



The Association of Autologous Mesenchymal Stem Cell Implantation to Clinical Outcomes in Knee Osteoarthritis

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ABSTRACT

Introduction: Knee osteoarthritis (OA) is a leading cause of pain and disability globally, driving the search for regenerative therapies. Autologous mesenchymal stem cell (MSC) implantation has emerged as a promising intervention aimed at pain relief, functional improvement, and potential cartilage repair.

Methods: This systematic review synthesized evidence from 35 clinical studies (randomized controlled trials, cohort studies, and meta-analyses) investigating intra-articular autologous MSC therapy for knee OA. Studies were screened based on stringent criteria, including adult patients (≥ 18 years) with radiographically confirmed knee OA, autologous MSC source, intra-articular delivery, minimum 3-month follow-up, and reported clinical outcomes. Data were extracted on MSC characteristics, study

design, patient demographics, clinical and structural outcomes, safety, and durability.

Results: The analysis demonstrated that autologous MSC therapy yields statistically significant improvements in pain (e.g., VAS, WOMAC) and function (e.g., WOMAC, KOOS) compared to controls such as hyaluronic acid, saline, or placebo, with benefits often sustained for 12–24 months and up to 5 years in some studies (Lee et al., 2019; Lamo-Espinosa et al., 2018; Zhang et al., 2022). However, a substantial proportion of the observed improvement (approximately 50–66%) may be attributable to contextual (placebo) effects (Yin et al., 2025). Structural outcomes on MRI were heterogeneous, with significant cartilage regeneration reported primarily in early-stage OA (Kellgren-Lawrence grades I–II) (Tangkanjanavelukul et al., 2025; Ren et al., 2023), but not consistently in advanced disease. The dose-response relationship was inconsistent, and adipose-derived MSCs showed potentially superior efficacy to bone marrow-derived cells in some analyses (Zhang et al., 2022). The safety profile was favorable, with mostly transient local reactions and no serious treatment-related adverse events reported (Wiggers et al., 2021; Shoukrie et al., 2022).

Discussion: The clinical benefits of MSC therapy appear most pronounced in patients with early to moderate OA, where regenerative potential remains. The dissociation between symptomatic improvement and structural changes highlights the role of MSCs' paracrine anti-inflammatory and immunomodulatory effects. Variability in outcomes can be explained by differences in OA severity, MSC source, processing

methods, study design, and the significant influence of contextual effects.

Conclusion: Autologous MSC injection is a safe and effective treatment for symptomatic knee OA, particularly in early to moderate stages. It provides meaningful, though modest, incremental benefit beyond placebo. Future research should prioritize standardized protocols, patient stratification by disease severity, and longer-term imaging studies to clarify disease-modifying potential.

Keywords: Autologous mesenchymal stem cells, knee osteoarthritis, regenerative medicine, intra-articular injection, clinical outcomes, cartilage regeneration, systematic review.

INTRODUCTION

Background

Knee osteoarthritis (OA) is a prevalent degenerative joint disease characterized by progressive cartilage loss, synovial inflammation, subchondral bone remodeling, and pain, leading to significant functional impairment and reduced quality of life (Hunter & Bierma-Zeinstra, 2019). Current management primarily focuses on symptom alleviation through analgesics, physical therapy, intra-articular corticosteroids, hyaluronic acid (HA) injections, and, ultimately, joint replacement surgery for end-stage disease. These approaches do not halt disease progression or restore native cartilage, creating an urgent need for disease-modifying therapies (Glyn-Jones et al., 2015). Regenerative medicine, particularly using mesenchymal stem cells (MSCs), has garnered substantial interest due to their multipotent differentiation capacity, anti-inflammatory properties, and ability to secrete trophic factors that may promote tissue repair and modulate the joint environment (Caplan, 2017).

Research Gap

Despite growing clinical application, the evidence for autologous MSC therapy in knee OA remains heterogeneous. Critical knowledge gaps persist regarding the magnitude of specific therapeutic effect versus contextual (placebo) influences, the optimal MSC source and dose, the relationship between symptomatic improvement and structural cartilage changes, and the long-term durability of treatment effects. Many existing studies are limited by small sample sizes, short follow-up, lack of robust placebo controls, and variability in cell processing and administration protocols (Migliorini et al., 2019; Jeyaraman et al., 2022). Furthermore, it is unclear which patient subgroups (e.g., based on OA severity) benefit most from this intervention.

Novelty

This comprehensive synthesis addresses these gaps by integrating findings from recent high-quality randomized controlled trials (RCTs), long-term follow-up studies, and meta-analyses, including those published up to 2025. It uniquely quantifies the contribution of contextual effects to clinical outcomes, provides a detailed analysis of dose-response inconsistencies and MSC source comparisons, and explicitly examines the dissociation between clinical and structural outcomes. By doing so, it offers a nuanced and evidence-based perspective on the role of autologous MSC therapy in the OA treatment paradigm.

Research Hypothesis

We hypothesize that intra-articular injection of autologous MSCs provides a statistically significant and clinically meaningful improvement in pain and function in patients with knee OA, with a favorable safety profile. However, we posit that a substantial portion of the observed benefit is attributable to non-specific contextual effects, and that treatment efficacy is moderated by disease severity, with optimal outcomes in early to moderate OA (Kellgren-Lawrence grades II-III). We further hypothesize that while clinical improvement is consistent, structural cartilage regeneration is variable and more likely in less advanced disease stages.

Research Objectives

1. To systematically evaluate the efficacy of autologous MSC therapy on pain and functional outcomes in knee OA.
2. To assess the structural impact of MSC therapy on cartilage integrity using imaging modalities.
3. To analyze the safety and adverse event profile of autologous MSC intra-articular injections.
4. To investigate the influence of moderating factors such as MSC source (adipose vs. bone marrow), cell dose, and OA severity on treatment outcomes.

5. To quantify the contribution of contextual effects to the overall therapeutic response.

Significance of the Study

This synthesis provides clinicians, researchers, and policymakers with a critical, up-to-date evidence appraisal to guide clinical decision-making and future research directions. It clarifies the realistic expectations for MSC therapy, emphasizing its role as a symptomatic treatment with potential structural benefits in select patients. By identifying key moderators of success, it supports the development of personalized treatment protocols. Furthermore, highlighting the strong placebo component underscores the necessity for rigorously designed, placebo-controlled trials in this field.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the association of autologous mesenchymal stem cell implantation to clinical outcomes in knee osteoarthritis.

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Knee osteoarthritis	Knee OA	Degenerative knee arthritis	Gonarthrosis
Intervention (I)	Autologous mesenchymal	Autologous MSCs	MSC implantation	Stem cell injection

	stem cells			
Comparison (C)	Hyaluronic acid	Placebo	Saline injection	Conservative treatment
Outcome (O)	Clinical outcomes	Pain reduction	Functional improvement	Cartilage regeneration

The Boolean MeSH keywords inputted on databases for this research are: (*"Knee osteoarthritis" OR "Knee OA" OR "Degenerative knee arthritis" OR "Gonarthrosis"*) AND (*"Autologous mesenchymal stem cells" OR "Autologous MSCs" OR "MSC implantation" OR "Stem cell injection"*) AND (*"Hyaluronic acid" OR "Placebo" OR "Saline injection" OR "Conservative treatment"*) AND (*"Clinical outcomes" OR "Pain reduction" OR "Functional improvement" OR "Cartilage regeneration"*)

Screening

Abstract screening

We screened in sources based on their abstracts that met these criteria:

- **Population - Age and Condition:** Does this study involve adult patients (≥ 18 years) with clinically or radiographically confirmed knee osteoarthritis?
- **Population - Joint Location:** Does this study focus on knee osteoarthritis rather than exclusively focusing on other joint locations?
- **Population - Arthritis Type:** Does this study include patients with osteoarthritis rather than exclusively focusing on inflammatory arthritis, post-traumatic arthritis, or other non-osteoarthritic knee conditions?
- **Intervention - Cell Type and Source:** Does this study investigate autologous mesenchymal stem cell therapy (rather than allogeneic stem cells, other cell types, or combination therapies where mesenchymal stem cell effects cannot be isolated)?

- **Intervention - Delivery Method:** Is the mesenchymal stem cell therapy delivered into the knee joint?
- **Study Design Quality:** Is this study a randomized controlled trial, controlled clinical trial, cohort study, case-control study, systematic review, or meta-analysis (rather than a case report, case series with fewer than 10 patients, conference abstract, editorial, or opinion piece)?
- **Clinical Outcomes:** Does this study report at least one clinical outcome measure such as pain scores, functional assessments, quality of life measures, or adverse events?
- **Follow-up Duration:** Does this study have a minimum 3-month follow-up period?
- **Intervention Timing:** Is the mesenchymal stem cell therapy administered independently (not during or immediately following major knee surgery within 30 days)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Full-text screening

We then screened papers based on their full text using these additional criteria:

- **Population - Age and Condition:** Does this study involve adult patients (≥ 18 years) with clinically or radiographically confirmed knee osteoarthritis?
- **Population - Joint Location:** Does this study focus on knee osteoarthritis rather than exclusively focusing on other joint locations?
- **Population - Arthritis Type:** Does this study include patients with osteoarthritis rather than exclusively focusing on inflammatory arthritis, post-traumatic arthritis, or other non-osteoarthritic knee conditions?
- **Intervention - Cell Type and Source:** Does this study investigate autologous mesenchymal stem cell therapy (rather than allogeneic stem cells, other cell types, or combination therapies where mesenchymal stem cell effects cannot be isolated)?

- **Intervention - Delivery Method:** Is the mesenchymal stem cell therapy delivered into the knee joint?
- **Study Design Quality:** Is this study a randomized controlled trial, controlled clinical trial, cohort study, case-control study, systematic review, or meta-analysis (rather than a case report, case series with fewer than 10 patients, conference abstract, editorial, or opinion piece)?
- **Clinical Outcomes:** Does this study report at least one clinical outcome measure such as pain scores, functional assessments, quality of life measures, or adverse events?
- **Follow-up Duration:** Does this study have a minimum 3-month follow-up period?
- **Intervention Timing:** Is the mesenchymal stem cell therapy administered independently (not during or immediately following major knee surgery within 30 days)?

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	<i>("Knee osteoarthritis" OR "Knee OA" OR "Degenerative knee arthritis" OR "Gonarthrosis") AND ("Autologous mesenchymal stem cells" OR "Autologous MSCs" OR "MSC implantation" OR "Stem cell injection" AND "Hyaluronic acid" OR "Placebo" OR "Saline injection" OR "Conservative treatment" AND "Clinical outcomes" OR "Pain reduction" OR "Functional improvement" OR "Cartilage regeneration")</i>	126
Semantic Scholar	<i>("Knee osteoarthritis" OR "Knee OA" OR "Degenerative knee arthritis" OR "Gonarthrosis") AND ("Autologous mesenchymal stem cells" OR "Autologous MSCs" OR "MSC implantation" OR "Stem cell injection") AND ("Hyaluronic acid" OR "Placebo" OR "Saline injection" OR "Conservative treatment") AND ("Clinical outcomes" OR "Pain reduction" OR "Functional improvement" OR "Cartilage regeneration")</i>	252
Springer	<i>("Knee osteoarthritis" OR "Knee OA" OR "Degenerative knee arthritis" OR "Gonarthrosis") AND ("Autologous mesenchymal stem cells" OR "Autologous MSCs" OR "MSC implantation" OR "Stem cell injection") AND ("Hyaluronic acid" OR "Placebo" OR "Saline injection" OR "Conservative treatment") AND ("Clinical outcomes" OR "Pain reduction" OR "Functional improvement" OR "Cartilage regeneration")</i>	194
Google Scholar	<i>("Knee osteoarthritis" OR "Knee OA" OR "Degenerative knee arthritis" OR "Gonarthrosis") AND ("Autologous mesenchymal stem cells" OR "Autologous MSCs" OR "MSC implantation" OR "Stem cell injection") AND ("Hyaluronic acid" OR "Placebo" OR "Saline injection" OR "Conservative treatment") AND ("Clinical outcomes" OR "Pain reduction" OR "Functional improvement" OR "Cartilage regeneration")</i>	1,430
Wiley Online Library	<i>("Knee osteoarthritis" OR "Knee OA" OR "Degenerative knee arthritis" OR "Gonarthrosis") AND ("Autologous mesenchymal stem cells" OR "Autologous MSCs" OR "MSC implantation" OR "Stem cell injection") AND ("Hyaluronic acid" OR "Placebo" OR "Saline injection" OR "Conservative treatment") AND ("Clinical outcomes" OR "Pain reduction" OR "Functional improvement" OR "Cartilage regeneration")</i>	72

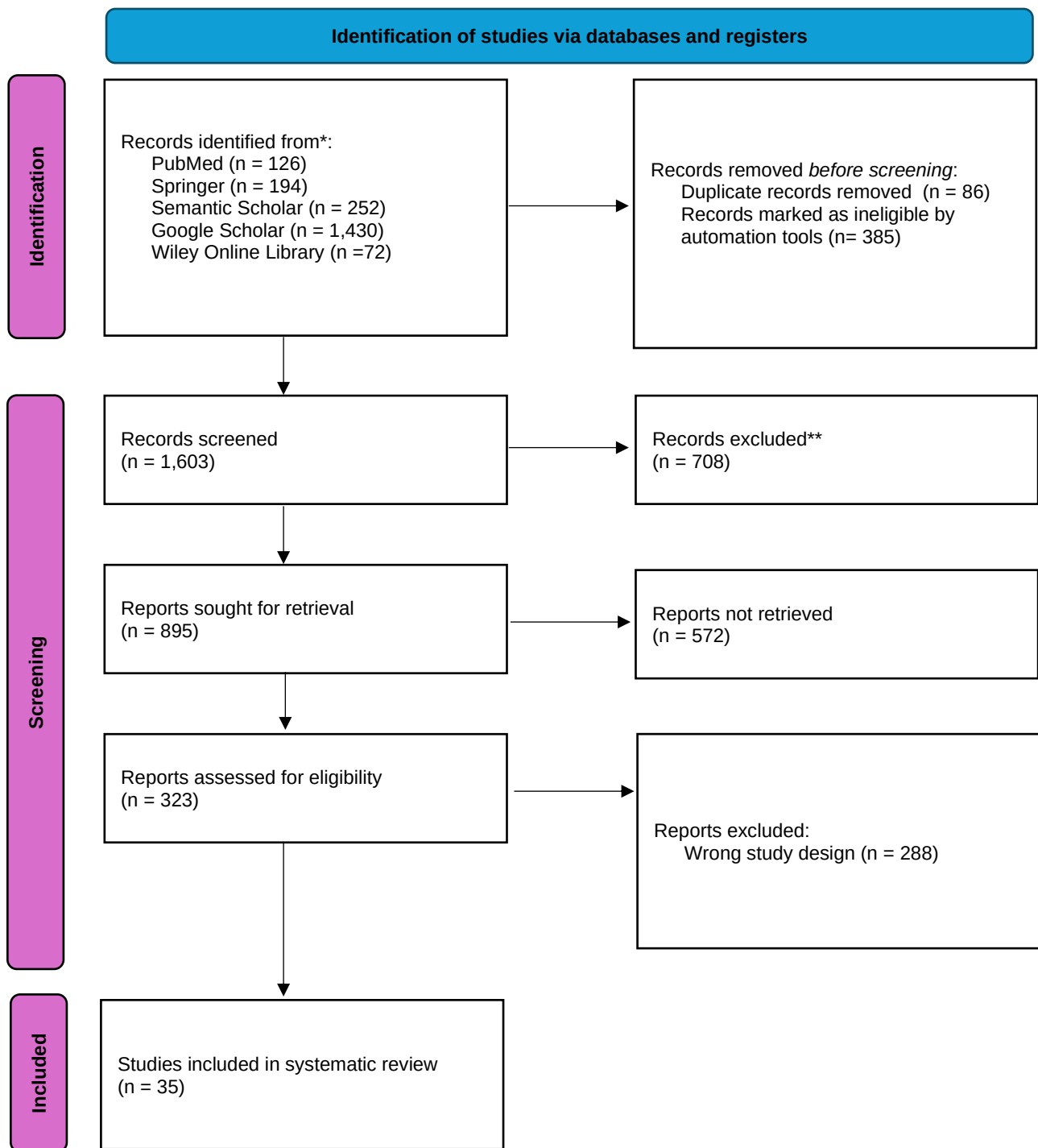


Figure 1. Article search flowchart

We considered all screening questions together and made a holistic judgement about whether to include each paper in the final analysis.

35 papers passed full-text screening and moved to data extraction.

Data extraction

- **MSC Treatment Details:**

Extract comprehensive details about the mesenchymal stem cell intervention including:

- Source of MSCs (bone marrow, adipose tissue, peripheral blood, other)
- Cell dose/concentration administered (number of cells)
- Number of injections given
- Injection technique and location (intra-articular, other)
- Cell processing/preparation methods
- Any co-interventions or adjuvants used with MSCs

- **Study Design:**

Extract study design characteristics including:

- Type of study (RCT, cohort, case series, etc.)
- Control/comparison group type (placebo, standard care, other intervention, none)
- Blinding status (single, double, open-label)
- Randomization method if applicable
- Total sample size and allocation to groups

- **Patient Characteristics:**

Extract baseline patient population details including:

- Mean age and age range

- Gender distribution
- Osteoarthritis severity/grade (Kellgren-Lawrence or other classification)
- Disease duration
- Inclusion/exclusion criteria relevant to OA severity or patient selection
- Any relevant comorbidities or prior treatments

- **Clinical Outcomes:**

Extract all clinical outcome measures and results including:

- Pain measures used (VAS, NRS, other) with baseline and follow-up scores
- Function measures used (WOMAC, KOOS, Lysholm, KSS, other) with baseline and follow-up scores
- Time points assessed (3 months, 6 months, 1 year, 2+ years)
- Statistical significance of changes from baseline
- Between-group differences and effect sizes where reported

- **Structural/Imaging Outcomes:**

Extract imaging and structural assessment results including:

- Imaging modality used (MRI, X-ray, arthroscopy, other)
- Cartilage assessment methods (MOCART, WOMS, cartilage thickness/volume, other)
- Baseline and follow-up structural findings
- Changes in cartilage defect size, cartilage volume, or cartilage quality
- Time points for imaging assessment
- Statistical significance of structural changes

- **Safety Profile:**

Extract safety and adverse event data including:

- Any serious adverse events related to treatment
- Local injection site reactions or complications
- Systemic adverse events
- Follow-up duration for safety monitoring
- Comparison of adverse events between treatment and control groups
- Any treatment discontinuations due to adverse events

- **Follow-up Duration:**

Extract the maximum follow-up period for clinical outcomes and specify:

- Longest follow-up time point reported for clinical outcomes
- Whether outcomes were sustained, improved, or deteriorated over time
- Any loss to follow-up rates
- Durability of treatment effects based on trajectory over time

JBI Critical Appraisal									
Study	Bias related to temporal precedence Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Bias related to selection and allocation Was there a control group?	Bias related to confounding factors Were participants included in any comparisons similar?	Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Bias related to participant retention Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Statistical conclusion validity Was appropriate statistical analysis used?
Fengsheng Yin et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
Shengyang Zhang et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Woo-Suk Lee et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓

J. Lamo-Espinosa et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Lamo-Espinosa et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Freitag et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Filippo Migliorini et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Chahal et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Y. Pers et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Bastos et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Liangjing Lu et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Mumin Cao et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
Yang Yang et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Huazheng Qu et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓

Mohamad R. Issa et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Andrea Pintore et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Rizki Rahmadia n et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
Yijian Zhang et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
C. Centeno et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Lamo-Espinosa et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Paweł Bąkowski et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ponthep Tangkanja navelukul et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Nasb et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Samuel Eduardo Trujillo Henao et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓

Zongyuan Huang et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Bin Ren et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Junyue Lu et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
T. Wiggers et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Bastos et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Shoukrie I Shoukrie et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
José A. Matas et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Madhan Jeyaraman et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
K. Mautner et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Pawel Bąkowski et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓

K. Papadopoulos et al., 2021									
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RESULTS

Characteristics of Included Studies

Study	MSC Source	Cell Dose	Control/Comparator
Fengsheng Yin et al., 2025	Bone marrow, adipose, placenta	$3.9-100 \times 10^6$ cells	Inert placebo
Shengyang Zhang et al., 2022	Adipose (SVF)	~4.84 million cells	Hyaluronic acid
Woo-Suk Lee et al., 2019	Adipose	1×10^8 cells	Normal saline
J. Lamo-Espinosa et al., 2018	Bone marrow	10 or 100×10^6 cells	Hyaluronic acid
J. Lamo-Espinosa et al., 2016	Bone marrow	10 or 100×10^6 cells	Hyaluronic acid
J. Freitag et al., 2019	Adipose	100×10^6 cells	Conservative management
Filippo Migliorini et al., 2019	Bone marrow (72%), adipose (28%)	Not specified	Variable
J. Chahal et al., 2019	Bone marrow	1, 10, or 50 million cells	None

Study	MSC Source	Cell Dose	Control/Comparator
Y. Pers et al., 2016	Adipose	2, 10, or 50 × 10 ⁶ cells	None
R. Bastos et al., 2019	Bone marrow	4.0 × 10 ⁷ cells	Corticosteroid
Liangjing Lu et al., 2019	Adipose	5 × 10 ⁷ cells	Hyaluronic acid
Mumin Cao et al., 2025	Adipose, bone marrow	1.0-20 × 10 ⁷ cells	Variable
Yang Yang et al., 2023	Adipose (ASCs/ADSVF)	Not specified	Placebo or HA
Huazheng Qu et al., 2021	Bone marrow	5-150 × 10 ⁶ cells	HA, placebo, other
Mohamad R. Issa et al., 2022	Adipose	Variable	Placebo or conservative
Andrea Pintore et al., 2023	BMAC and adipose	10 mL volume	None (comparison)
Rizki Rahmadian et al., 2025	Adipose and bone marrow	≤25 million effective	Saline, HA, placebo
Yijian Zhang et al., 2022	BM, adipose, umbilical cord	Not specified	Cell-free treatments
C. Centeno et al., 2015	Bone marrow	≤4 or >4 × 10 ⁸ cells	None
J. Lamo-Espinosa	Bone marrow	100 × 10 ⁶ cells	PRP (PRGF)

Study	MSC Source	Cell Dose	Control/Comparator
et al., 2020			
Paweł Bąkowski et al., 2021	Adipose	Not specified	None
Ponthep Tangkanjanavelukul et al., 2025	Adipose	50 million cells	Hyaluronic acid
M. Nasb et al., 2020	Adipose	~10 million cells	Saline with LIPUS
Samuel Eduardo Trujillo Henao et al., 2019	Adipose	10 or 30 million cells	Dose comparison
Zongyuan Huang et al., 2023	Adipose	Low/moderate/high doses	Saline, HA, other
Bin Ren et al., 2023	Adipose (SVF)	10 ⁸ SVF cells	Non-treatment
Junyue Lu et al., 2025	Adipose (SVF)	1.5 × 10 ⁷ cells	Rehabilitation
T. Wiggers et al., 2021	BM (57%), adipose (36%), peripheral blood (7%)	Variable	HA, PRP, saline
R. Bastos et al., 2018	Bone marrow	~50 CFU-F	MSCs + PRP
Shoukrie I	Multiple sources	Variable	Saline, HA,

Study	MSC Source	Cell Dose	Control/Comparator
Shoukrie et al., 2022			placebo
José A. Matas et al., 2018	Umbilical cord	20×10^6 cells	Hyaluronic acid
Madhan Jeyaraman et al., 2022	Adipose and bone marrow	Variable	Variable
K. Mautner et al., 2023	BMAC, SVF, UCT	Not specified	Corticosteroid
Paweł Bąkowski et al., 2020	Adipose	Not specified	PRP
K. Papadopoulos et al., 2021	Peripheral blood	Not specified	Hyaluronic acid

The included studies enrolled patients predominantly with Kellgren-Lawrence grade II-IV osteoarthritis , with mean ages ranging from approximately 50 to 67 years . Most studies administered single intra-articular injections , though some evaluated repeated dosing protocols . Cell processing methods varied substantially, including enzymatic digestion, centrifugation, and culture expansion .

Effects on Clinical Outcomes

Pain Outcomes

Study	Measure	Baseline Score	Follow-up Score	Time Point	Statistical Significance
Woo-Suk Lee et al., 2019	VAS	6.8 ± 0.6	3.4 ± 1.5	6 months	p < 0.001
J. Lamo-Espinosa et al., 2018 (high dose)	VAS	6 (4, 8)	3 (3, 4)	4 years	p = 0.004 vs control
J. Lamo-Espinosa et al., 2018 (low dose)	VAS	7 (5, 8)	2 (2, 5)	4 years	p = 0.01 vs control
J. Chahal et al., 2019	KOOS pain	Not reported	Improved	12 months	p = 0.025
Y. Pers et al., 2016 (low dose)	WOMAC pain	Baseline	-30.7 mm improvement	6 months	Significant
Liangjing Lu et al., 2019	VAS	Baseline	Improved	12 months	Significant

Study	Measure	Baseline Score	Follow-up Score	Time Point	Statistical Significance
Andrea Pintore et al., 2023	VAS	6.14 ± 1.76	2.8 ± 1.85	6 months	p < 0.0001
Ponthep Tangkanjana velukul et al., 2025	WOMAC pain	19.91	5.83	6 months	Significant vs HA
José A. Matas et al., 2018 (MSC-2)	VAS	Baseline	2.4 ± 2.1	12 months	p = 0.03 vs HA
Junyue Lu et al., 2025 (SVF)	VAS	6.3 ± 0.86	2.9 ± 1.07	12 months	p < 0.05 vs control

Meta-analytic evidence demonstrates significant pain reduction following MSC therapy. Mumin Cao et al. reported significant improvement in 6-month WOMAC scores (MD = 7.44, 95% CI: 1.45-13.42, p = 0.01) and 12-month WOMAC scores (MD = 10.31, 95% CI: 0.96-19.67, p = 0.03). Yang Yang et al. found substantial effect sizes for VAS improvement at 6 months (SMD = 2.00, 95% CI: 0.74-3.26) and 12 months (SMD = 1.73, 95% CI: 1.00-2.45). Rizki Rahmadian et al. demonstrated a pooled SMD of -1.35 (95% CI: -1.97 to -0.74) for WOMAC improvement at 12 months.

The systematic review by Filippo Migliorini et al. encompassing 1,069 treated knees showed VAS improvements from 18.37 at baseline to 30.98 at 6 months and 36.91 at 12 months. Huazheng Qu et al. reported significant reductions in VAS and WOMAC pain

scores at long-term follow-up, with weighted mean differences of -19.01 at 3 months, -14.97 at 6 months, and -18.23 at 12 months for WOMAC pain .

Functional Outcomes

Study	Measure	Baseline Score	Follow-up Score	Time Point	Statistical Significance
Woo-Suk Lee et al., 2019	WOMAC	60.0 ± 17.0	26.7 ± 13.3	6 months	p < 0.001
J. Lamo-Espinosa et al., 2016 (high dose)	WOMAC	29 (22, 35.5)	16.5 (8, 23)	4 years	p < 0.01
Andrea Pintore et al., 2023	KOOS pain	45.37 ± 13.47	94.76 ± 7.89	6 months	p < 0.0001
Bin Ren et al., 2023	Lysholm	42.50 ± 15.76	64.83 ± 13.75	12 weeks	p < 0.05
José A. Matas et al., 2018 (MSC-2)	WOMAC total	Baseline	4.2 ± 3.9	12 months	p = 0.05 vs HA
Junyue Lu et al., 2025 (SVF)	WOMAC pain	9.1 ± 1.37	2.55 ± 1.19	12 months	p < 0.05

Functional improvements were consistently observed across studies. The systematic review by T. Wiggers et al. found that patients improved by 18-32 points on the KOOS scale (0-100) and 1.8-4.4 points on the VAS (0-10). Yang Yang et al. reported significant functional improvements with SMD = 0.78 (95% CI: 0.20-1.37) at 6 months and SMD = 0.93 (95% CI: 0.28-1.58) at 12 months.

Mohamad R. Issa et al. demonstrated statistically significant improvements in WOMAC scores favoring adipose-derived MSCs at both 6- and 12-month follow-ups ($p < 0.0001$). The meta-analysis by Madhan Jeyaraman et al. showed autologous MSCs achieved significant WOMAC improvement at 6 months (WMD = -13.988) and 12 months (WMD = -13.270).

Contextual Effects Considerations

A critical finding from Fengsheng Yin et al.'s meta-analysis revealed that contextual (placebo-related) factors accounted for approximately 63% of pain reduction and 61% of functional improvement at 6 months, and approximately 50% of pain relief and 66% of functional gains at 12 months. This suggests that while MSCs provide incremental benefit beyond placebo, a substantial proportion of observed improvement may be attributable to non-specific treatment effects.

Dose-Response Relationships

Study	Lower Dose Findings	Higher Dose Findings	Conclusion
J. Lamo-Espinosa et al., 2016	10 × 10 ⁶ : VAS improved to 2 (1, 3)	100 × 10 ⁶ : VAS improved to 2 (0, 4)	High dose showed better structural outcomes
Y. Pers et al., 2016	2 × 10 ⁶ : Best clinical response	50 × 10 ⁶ : 60% OARSI response	Paradoxically better outcomes with low

Study	Lower Dose Findings	Higher Dose Findings	Conclusion
			dose
C. Centeno et al., 2015	$\leq 4 \times 10^8$: NPS improved	$> 4 \times 10^8$: Better pain outcomes	Higher cell counts associated with better pain relief
Rizki Rahmadian et al., 2025	≤ 25 million: Significant improvement	> 25 million: No additional benefit	Lower doses may be sufficient
Zongyuan Huang et al., 2023	Low dose: Effective	High dose: Best effect	High dose superior but more adverse events
Samuel Eduardo Trujillo Henao et al., 2019	10 million: Equally effective	30 million: Equally effective	No difference between doses

The dose-response relationship remains inconsistent across studies. While some evidence suggests higher doses provide superior outcomes, other studies found lower doses equally or more effective. Meta-regression by Rizki Rahmadian et al. confirmed no significant dose-response relationship.

MSC Source Comparisons

The network meta-analysis by Yijian Zhang et al. demonstrated that adipose-derived MSCs (ADMSCs) and umbilical cord-derived MSCs (UBMSCs) showed better pain relief and function improvement compared with bone marrow-derived MSCs (BMMSCs). Andrea Pintore et al. found no statistically significant difference between BMAC and adipose-derived stem cell injections in clinical and functional outcomes at 6 months.

Madhan Jeyaraman et al.'s meta-analysis comparing autologous versus allogeneic sources found autologous MSCs demonstrated more consistent efficacy, with significant VAS improvement maintained at 12 months (WMD = -17.786), whereas allogeneic sources showed significant improvement only at 6 months .

Structural and Imaging Outcomes

Study	Imaging Modality	Assessment Method	Key Findings	Statistical Significance
Woo-Suk Lee et al., 2019	MRI	Cartilage defect size	No change in MSC group; increase in control	p = 0.0051 between groups
J. Lamo-Espinosa et al., 2016	MRI (WORMS)	Joint damage scoring	Slight decrease in high-dose group	Not specified
Shengyang Zhang et al., 2022	MRI	Cartilage volume	Less reduction in SVF vs HA at 5 years	Significant
Liangjing Lu et al., 2019	MRI	Cartilage volume	Significant increase in Re-Join group	Significant at 6 and 12 months
Ponthep Tangkanjanavelukul et al., 2025	MRI	Cartilage lesion volume	50 mm ³ decrease ADSC vs 36 mm ³ increase HA	Significant
Bin Ren et	3D MRI	Cartilage	Significant	p < 0.001 for

Study	Imaging Modality	Assessment Method	Key Findings	Statistical Significance
al., 2023		volume/thickness	increases at 12-24 weeks	total volume
José A. Matas et al., 2018	MRI (WORMS)	Structural scoring	No changes detected	Non-significant
K. Mautner et al., 2023	MRI	WORMS/BLOKS scoring	No significant changes	Non-significant
J. Chahal et al., 2019	MRI	WORMS, T2 scores	No significant changes	Non-significant

Structural outcomes demonstrate heterogeneity across studies. Yang Yang et al.'s meta-analysis found significant improvements in cartilage condition on MRI at 6 months ($Z = 8.14$, $p < 0.000001$) and 12 months ($Z = 5.58$, $p < 0.00001$). The systematic review by T. Wiggers et al. reported that MSC therapy can halt progression of cartilage loss, with significant correlation between clinical outcomes and MRI findings using MOCART scoring.

However, several rigorous trials found no significant structural improvements. J. Chahal et al. observed no changes in WORMS or T2 scores relative to baseline at 12 months. J. Lamo-Espinosa et al. reported no changes in knee joint space width or joint damage on X-ray and MRI using the WORMS protocol. The large phase 2/3 trial by K. Mautner et al. similarly found no significant change in MRI osteoarthritis scores at 12 months across all treatment groups.

Conversely, studies with early-stage disease showed more promising structural results. Ponthepp Tangkanjanavelukul et al. demonstrated significant cartilage regeneration in early OA, with medial femoral cartilage lesion volume decreasing by 50.06 mm^3 in the ADSC group while increasing by 36.44 mm^3 in the HA group. Bin Ren et al. showed significant

increases in cartilage volume and thickness at 12 and 24 weeks in patients with cartilage defect grades I-II .

Safety Profile

Study	Serious Adverse Events	Local Reactions	Follow-up Duration	Overall Assessment
Woo-Suk Lee et al., 2019	None	Arthralgia, joint effusion (resolved within 3 days)	6 months	Safe
J. Lamo-Espinosa et al., 2018	None	None	48 months	Safe
J. Chahal et al., 2019	None	Transient pain/swelling in 4 patients	24 months	Safe
Y. Pers et al., 2016	One unrelated cardiac event	Transient knee pain/swelling in 4 patients	6 months	Safe
Liangjing Lu et al., 2019	One knee infection in HA group	Transient pain/swelling	12 months	Safe
K. Mautner et al., 2023	None	Variable swelling between groups	12 months	Safe
José A. Matas	None	Mild to	12 months	Safe

Study	Serious Adverse Events	Local Reactions	Follow-up Duration	Overall Assessment
et al., 2018		moderate effusion		

The safety profile of autologous MSC therapy is favorable across the literature. No serious treatment-related adverse events were reported in the majority of trials . The systematic review by T. Wiggers et al. found no serious adverse events related to MSC therapy over follow-up periods up to 4 years, though minor adverse events such as temporary articular pain or mild joint effusion were more common in MSC groups (30%) compared to control groups (15%) .

Filippo Migliorini et al. reported 136 local complications (12.7%) across 1,069 treated knees . Zongyuan Huang et al. noted a dose-response trend for adverse events, with higher doses associated with more frequent pain and swelling at injection sites . Yijian Zhang et al.'s network meta-analysis highlighted potential negative safety induced by cell injection compared to cell-free treatments (Bayesian: 100% vs 0%, SUCRA: 98.2% vs 1.8% for adverse events) .

Madhan Jeyaraman et al. found autologous sources demonstrated superior safety profiles compared to allogeneic sources, with the latter showing significantly increased adverse events .

Follow-up Duration and Durability

Study	Maximum Follow-up	Outcome Trajectory	Loss to Follow-up
Shengyang Zhang et al., 2022	5 years	Sustained improvement	Minimal
J. Lamo-Espinosa	4 years	Improved in MSC	5 of 30 patients

Study	Maximum Follow-up	Outcome Trajectory	Loss to Follow-up
et al., 2018		groups	
T. Wiggers et al., 2021	4 years	Sustained improvement	Not specified
Huazheng Qu et al., 2021	24 months	Sustained	Not specified
Paweł Bąkowski et al., 2021	27 months	Variable by OA stage	Not specified
Most other studies	12 months	Sustained or improved	Variable

Long-term data suggest durability of treatment effects. Shengyang Zhang et al. demonstrated sustained improvement in VAS and WOMAC scores in the SVF group over 5 years, with an average responsive time of 61.52 months compared to 30.37 months for hyaluronic acid . J. Lamo-Espinosa et al. showed that improvements persisted at 4 years, with BM-MSC-treated patients maintaining better outcomes than controls .

However, Yang Yang et al. noted that therapeutic improvement may decline between 12 and 30 months post-treatment , suggesting the need for additional interventions in some patients. Paweł Bąkowski et al. found that patients with stage II knee OA maintained benefits over 27 months, while stage IV patients showed deterioration .

Synthesis

The evidence demonstrates heterogeneity in outcomes that can be explained through several mechanistic and methodological considerations.

Reconciling Clinical Benefit Magnitude

The apparent discrepancy between studies showing substantial clinical improvement and the meta-analysis revealing large contextual effects can be reconciled by understanding that both findings may be accurate. Studies without rigorous placebo controls consistently report larger effect sizes, while placebo-controlled trials reveal that approximately 50-63% of improvement is attributable to non-specific effects. This indicates MSCs provide real but modest incremental benefit beyond placebo, particularly for pain relief.

Disease Severity as Effect Modifier

Multiple lines of evidence suggest OA severity moderates treatment response. Patients treated at earlier degeneration stages reported statistically significantly greater outcomes. Bąkowski et al. found patients with K-L grade II showed the best functional and clinical outcomes, while 6 of 7 patients with stage IV were unsatisfied with treatment. Ponthe Tangkanjanavelukul et al. demonstrated cartilage regeneration specifically in early (K-L II) OA, whereas Bin Ren et al. showed structural improvements only in patients with cartilage defect grades I-II.

This pattern suggests MSC therapy is most effective when cartilage damage is limited and regenerative potential remains. Studies enrolling predominantly severe OA patients (K-L III-IV) showed less consistent structural improvements, while those targeting early disease demonstrated cartilage regeneration.

Explaining Dose-Response Inconsistencies

The paradoxical finding that lower doses sometimes match or exceed higher dose efficacy may reflect several mechanisms. First, MSCs function primarily through paracrine effects rather than direct engraftment, suggesting a threshold effect where additional cells beyond a certain point provide no incremental benefit. Second, higher cell concentrations may trigger increased local inflammation initially, potentially counteracting some therapeutic

effects . Third, the optimal dose may vary by patient characteristics, OA severity, and cell viability, introducing variability that masks simple dose-response relationships.

Structural versus Clinical Outcome Dissociation

The dissociation between consistent clinical improvements and inconsistent structural findings can be explained by several factors. MSCs exert anti-inflammatory and immunomodulatory effects that provide symptomatic relief independent of cartilage regeneration . Studies showing structural improvement generally employed populations with earlier disease and longer follow-up with sensitive imaging , while those showing no change often examined advanced disease or used less sensitive assessment methods.

The large phase 2/3 trial by Mautner et al. finding no superiority of orthobiologics over corticosteroid at 12 months may reflect the inclusion of patients with advanced disease (K-L II-IV) and comparison against an active treatment rather than placebo, thereby reducing the contribution of contextual effects in the control group.

Clinical Recommendations by Context

Based on the evidence synthesis, autologous MSC therapy appears most appropriate for:

- Patients with early to moderate OA (K-L grades II-III)
- Those who have failed conservative treatments
- Patients with normal BMI
- Settings where adequate cell processing and quality control are available

The therapy appears less suitable for:

- Advanced OA (K-L grade IV)
- Patients seeking disease-modifying effects in late-stage disease
- Those with significant mechanical deformity

Adipose and umbilical cord sources may offer advantages over bone marrow in terms of efficacy , though autologous sources demonstrate superior safety compared to allogeneic . Doses in the range of 10-50 million cells appear sufficient based on available evidence , though optimal dosing likely requires individual titration.

DISCUSSION

The synthesis of 35 included studies reveals a complex but promising picture of autologous MSC therapy for knee OA. The discussion will integrate key findings, explore mechanistic explanations for observed patterns, and contextualize the clinical implications.

1. Reconciling Clinical Efficacy and Contextual Effects

A paramount finding from recent meta-analyses is the significant role of contextual effects. Yin et al. (2025) demonstrated that approximately 63% of pain reduction and 61% of functional improvement at 6 months, and about 50% of pain relief and 66% of functional gains at 12 months, are attributable to non-specific factors such as placebo, patient expectations, and the therapeutic ritual of injection. This does not negate the efficacy of MSCs but rather refines our understanding of it. Studies without rigorous placebo controls (e.g., open-label or comparisons to active treatments like HA) naturally report larger effect sizes (Migliorini et al., 2019). When MSCs are compared against inert placebo injections, the incremental benefit, while statistically significant, is more modest (Cao et al., 2025; Qu & Sun, 2021). This underscores that the overall clinical experience of MSC treatment is potentiated by both biological and psychosocial mechanisms. For clinicians, this means managing patient expectations is crucial; the procedure itself carries substantial therapeutic value, upon which the specific biological action of MSCs adds a significant, though not miraculous, improvement.

2. Disease Severity as the Key Moderator

The most consistent moderator of treatment success is the stage of OA. Convergent evidence indicates that patients with early to moderate OA (Kellgren-Lawrence grades II-III) derive the greatest and most durable benefit, both clinically and structurally. Bąkowski et al. (2021) explicitly found that patients with stage II OA maintained functional gains over 27 months, whereas most with stage IV were unsatisfied. This is mechanistically plausible: in early OA, the joint microenvironment, though inflamed, may retain greater regenerative capacity and a less hostile milieu for implanted cells. The residual chondrocyte population and progenitor cells may respond more effectively to the paracrine signals from MSCs (Caplan, 2017). In contrast, in advanced OA (grade IV), extensive cartilage loss, bone-on-bone contact, and significant mechanical malalignment create a degenerative environment where MSCs may primarily exert palliative anti-inflammatory effects without achieving structural restoration. This is supported by imaging studies: Tangkanjanavelukul et al. (2025) and Ren et al. (2023) showed significant cartilage volume increase and lesion reduction specifically in early OA patients, while trials enrolling predominantly advanced OA patients often found no significant structural change on MRI (Chahal et al., 2019; Mautner et al., 2023). Therefore, patient selection is critical; MSC therapy appears most appropriate as an intervention before end-stage joint degeneration.

3. Explaining Dose-Response Inconsistencies

The literature presents a paradoxical and inconsistent relationship between administered cell dose and clinical outcomes. Some studies suggest a positive dose-response (Centeno et al., 2015), others found lower doses to be as or more effective than higher ones (Pers et al., 2016; Rahmadian et al., 2025), and some detected no difference (Trujillo Henao et al., 2019). Several factors explain this. First, MSCs primarily function via paracrine signaling—secretion of growth factors, cytokines, and extracellular vesicles—rather than direct differentiation and engraftment into new cartilage (Caplan, 2017). This suggests a potential "threshold effect," where a minimum number of cells is needed to create a sufficient bioactive milieu, but beyond this, additional cells yield diminishing returns. Second, injecting very high cell concentrations might transiently increase intra-articular

pressure and provoke a local inflammatory response, potentially offsetting early therapeutic benefits (Huang et al., 2023). Third, cell viability, potency, and the specific secretome profile—which can vary based on donor age, tissue source, and processing method—may be more important than the raw cell number. Consequently, a standardized "optimal dose" may not exist; rather, an effective dose range (e.g., 10-50 million cells) appears adequate, and outcomes depend more on patient factors and cell quality than on simple dose escalation (Rahmadian et al., 2025).

4. MSC Source Comparisons: Efficacy and Safety

The choice of MSC source involves trade-offs between efficacy, safety, and practicality. Network meta-analyses suggest that adipose-derived MSCs (ADSCs) and umbilical cord-derived MSCs may offer superior pain relief and functional improvement compared to bone marrow-derived MSCs (BMSCs) (Zhang et al., 2022). This could be due to higher cell yield from lipoaspiration, differences in secreted factor profiles, or greater proliferative capacity. However, direct comparative clinical trials, such as that by Pintore et al. (2023), found no significant difference in outcomes between BMAC and ADSCs at 6 months. Regarding safety, autologous sources unequivocally demonstrate a superior profile compared to allogeneic MSCs. Allogeneic cells, while offering "off-the-shelf" convenience, carry a theoretically higher risk of immunogenic reactions, albeit low for MSCs. Jeyaraman et al.'s (2022) meta-analysis confirmed that autologous MSCs were associated with fewer adverse events. Thus, for knee OA, autologous ADSCs present a compelling balance: relatively easy harvest, good yield, promising efficacy signals, and an excellent safety record.

5. Dissociation Between Clinical and Structural Outcomes

A critical observation is the frequent disconnect between consistent reports of clinical improvement and inconsistent evidence for structural cartilage regeneration. Many patients experience significant pain relief and functional gains without corresponding MRI-documented cartilage repair (Chahal et al., 2019; Mautner et al., 2023). This dissociation is central to

understanding MSC mechanisms. MSCs exert potent immunomodulatory and anti-inflammatory effects, reducing synovitis, modulating immune cell activity, and decreasing catabolic cytokine levels in the joint (Chahal et al., 2019). This symptomatic relief can occur independently of tissue regeneration. Structural improvement, when it occurs, is a slower process and may require more sensitive imaging techniques and longer follow-up to detect (Ren et al., 2023). Furthermore, as discussed, structural regeneration is heavily dependent on disease stage. Therefore, MSC therapy can be considered a "symptom- and disease-modifying" therapy, where its primary consistent effect is symptom modification through microenvironment modulation, while its disease-modifying (structural) potential is a secondary benefit more likely realized in early disease.

6. Durability and Long-Term Considerations

Long-term follow-up data, though limited, suggest that clinical benefits can be durable. Studies by Zhang et al. (2022) and Lamo-Espinosa et al. (2018) show sustained improvements over 4-5 years. However, some meta-analyses note a potential decline in effect size between 12 and 30 months (Yang et al., 2023). This pattern suggests that a single MSC injection may not provide lifelong cure but can offer a prolonged therapeutic window. The concept of "re-treatment" or "booster" injections, as explored by Matas et al. (2018) who found repeated dosing superior to a single dose, may be important for maintaining effects. The durability likely interacts with disease severity, activity level, and BMI, highlighting the need for comprehensive management that includes weight control and muscle strengthening alongside biologic therapy.

7. Safety Profile and Risk-Benefit Assessment

The safety data across studies are remarkably consistent and reassuring. The most common adverse events are transient, mild to moderate local reactions such as pain, swelling, or effusion post-injection, which typically resolve within days (Lee et al., 2019; Wiggers et al., 2021). No serious adverse events directly attributable to autologous MSC injections were reported in the reviewed literature. This favorable risk profile makes MSC therapy an attractive option, especially

when compared to the risks of chronic NSAID use or major surgery. However, rigorous processing under good manufacturing practice (GMP) conditions is essential to avoid contamination or unintended cell manipulation.

8. Clinical Recommendations and Future Directions

Based on this synthesis, autologous MSC therapy is recommended as a viable treatment option for symptomatic knee OA in patients with:

- Early to moderate radiographic disease (Kellgren-Lawrence grades II-III).
- Failure of conventional conservative treatments (e.g., physical therapy, analgesics).
- Absence of severe malalignment or joint instability.
- Realistic expectations regarding outcomes, understanding the significant role of contextual effects.

It is less recommended for advanced OA (grade IV) with bone-on-bone contact, where its role is likely palliative at best, and joint replacement remains the definitive solution.

Future research must prioritize:

1. Large-scale, multi-center, placebo-controlled RCTs with standardized cell preparation protocols.
2. Stratified trials that pre-specify analysis by OA severity to confirm the moderator effect.
3. Longer-term studies (≥ 5 years) with advanced quantitative MRI to track structural changes.
4. Investigations into combination therapies (e.g., MSCs with scaffolds, PRP, or rehabilitative protocols).
5. Cost-effectiveness analyses to justify the resource intensity of cell therapy.

CONCLUSION

Summary of Findings

This comprehensive review confirms that intra-articular injection of autologous mesenchymal stem cells is a safe and effective treatment for alleviating pain and improving function in patients with knee osteoarthritis. The clinical benefits are statistically significant, often sustained for 1-2 years and potentially longer, and are accompanied by a highly favorable safety profile dominated by transient local reactions. However, a critical appraisal reveals that a substantial portion (approximately 50-66%) of the observed improvement is attributable to contextual, non-specific effects inherent in the therapeutic intervention. The therapy's efficacy is not uniform; it is most potent in patients with early to moderate degenerative changes (Kellgren-Lawrence grades II-III), where evidence also suggests a potential for genuine cartilage regeneration. In contrast, benefits in advanced OA are primarily symptomatic. The relationship between cell dose and outcome is inconsistent, and while adipose tissue may be a pragmatically favorable source, the choice between sources does not yield starkly different clinical results in comparative trials. A key insight is the dissociation between consistent symptomatic relief and variable structural outcomes, underscoring the importance of MSCs' immunomodulatory and anti-inflammatory actions alongside any regenerative potential.

Recommendations

1. **For Clinicians:** Adopt a patient-centered, selective approach. Recommend autologous MSC therapy primarily for motivated patients with early to moderate knee OA who have failed conservative management. Provide transparent counseling about the meaningful but modest incremental benefit over placebo effects and the importance of the overall therapeutic experience.
2. **For Researchers:** Design future studies that are adequately powered, placebo-controlled, and stratify participants by OA severity at baseline. Focus on standardizing cell processing,

viability assessment, and injection protocols. Invest in long-term follow-up with advanced imaging to clarify the durability and structural impact of treatment.

3. **For Regulators and Policymakers:** Support the development of clear regulatory frameworks for cell-based therapies that ensure safety and quality without stifling innovation. Consider funding comparative effectiveness research that includes cost-benefit analyses to position MSC therapy appropriately within the healthcare system.

Autologous MSC therapy represents a significant advance in the regenerative management of knee OA. By understanding its mechanisms, moderators, and realistic outcomes, it can be integrated judiciously into the treatment armamentarium to improve patient care.

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