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# Efficacy of Dextrose Prolotherapy Compared with Intra-Articular Corticosteroids in Knee Osteoarthritis: A Systematic Review of Controlled Trials

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Pain.

**ABSTRACT**
Knee osteoarthritis (OA) is a leading cause of pain and disability in older adults worldwide. While intra-articular corticosteroid injections (IACIs) are widely used for short-term relief, dextrose prolotherapy has emerged as a regenerative alternative with potential for longer-term functional improvement, though direct comparative evidence remains limited. This study aims to systematically compare the clinical effectiveness of corticosteroid and dextrose prolotherapy injections in improving pain and physical function among knee OA patients. This systematic review followed the PRISMA 2020 statement. A comprehensive search of PubMed and ScienceDirect identified randomized controlled and prospective comparative trials published between January 2015 and October 2025, involving adults with radiographically or clinically confirmed knee OA reporting outcomes via validated scales (VAS, WOMAC, KOOS). Risk of bias was assessed using the Cochrane RoB 2.0 tool. From 724 records, 11 studies met inclusion criteria (six on prolotherapy, five on corticosteroids; sample sizes 40–484). Prolotherapy produced sustained pain and functional improvements at 8–12 weeks, persisting up to 6 months, while corticosteroids offered faster relief (1–4 weeks) but diminishing benefits after 3–6 months. Extended-release formulations (FX006, TLC599) provided modestly longer control. Both interventions were effective for mild-to-moderate knee OA; prolotherapy showed longer-lasting, safe, and cost-effective potential, warranting further high-quality trials.

## INTRODUCTION

Knee osteoarthritis (OA) is a leading cause of chronic pain, functional limitation, and reduced quality of life among older adults worldwide (Zhang & Jordan, 2010; GBD 2019 Diseases and Injuries Collaborators, 2020). The knee is the most commonly affected joint, with symptomatic knee OA affecting approximately 10% of men and 13% of women aged 60 years or older (Zhang & Jordan, 2010). With rising life expectancy and an aging population, the socioeconomic and disability burden attributable to knee OA is expected to increase substantially in the coming decades (Vos et al., 2020). A 2020 Global Burden of Disease (GBD) analysis estimated that approximately 595 million people were living with osteoarthritis worldwide with knee OA accounting for the majority of disability-adjusted life years (DALYs) and projections indicate an increase of more than 74.9% in global knee OA cases by 2050, underscoring its growing public health impact (Vos et al., 2020). Non-surgical management

remains the mainstay of therapy for knee OA, particularly in elderly patients, and aims primarily at symptom relief, preservation of function, and delaying or avoiding joint replacement (Bannuru et al., 2019). Current international guidelines including those from the Osteoarthritis Research Society International (OARSI), the American College of Rheumatology (ACR), and the European League Against Rheumatism (EULAR) recommend a stepwise approach emphasizing patient education, weight management, exercise therapy, and judicious use of pharmacologic or injection-based modalities before surgical options are considered (Bannuru et al., 2019; Kolasinski et al., 2020; Fernandes et al., 2013).

Among minimally invasive options, intra-articular corticosteroid injections (IACIs) are commonly employed to reduce pain and inflammation during symptomatic flares of knee osteoarthritis (OA) (Jones et al., 2019; Testa et al., 2021). Current clinical guidelines from the American College of Rheumatology (ACR), the European League Against Rheumatism (EULAR), and the Osteoarthritis Research Society International (OARSI) recommend corticosteroid injections with caution, often limiting their use to three or four injections per year due to potential risks to joint structures (Bannuru et al., 2019; Kolasinski et al., 2020; Fernandes et al., 2013). Randomized controlled trials and meta-analyses have consistently demonstrated that IACIs provide significant short-term pain relief, typically lasting 2–4 weeks, with some studies reporting modest benefits extending up to 12–24 weeks in selected patient groups (Guermazi et al., 2023; Gupta et al., 2025; Pavone et al., 2021). However, the durability of symptom relief remains limited, and repeated injections may be associated with diminishing efficacy over time (Gupta et al., 2025; Pavone et al., 2021).

Recent observational studies have raised concerns regarding potential structural harm related to recurrent corticosteroid injections. Zeng et al. (2019) found that continuous IACI use was associated with increased odds of radiographic progression compared with non-users. Similarly, Bensa et al. (2024) reported MRI evidence of greater cartilage volume loss over two years in patients receiving corticosteroid injections compared with controls. Conversely, a nested case-control MRI study by Pelletier et al. (2020) suggested that a single intra-articular corticosteroid injection may induce transient meniscal thinning but did not demonstrate consistent long-term cartilage damage.

Despite these concerns, IACIs remain widely used in clinical practice due to their accessibility, cost-effectiveness, and rapid symptom relief. Nevertheless, the balance between symptomatic benefit and potential adverse effects on joint structures particularly in elderly patients with advanced degenerative changes remains an area of active debate (Bensa et al., 2024; Pelletier et al., 2020; Park et al., 2025; Deyle et al., 2020).

In parallel, dextrose prolotherapy has emerged as a regenerative or reparative injection therapy for chronic musculoskeletal disorders, including knee osteoarthritis (OA). The rationale of prolotherapy is that hypertonic dextrose induces a controlled inflammatory response that stimulates tissue healing, collagen synthesis, and remodelling of ligaments, tendons, and periarticular soft tissues (Reeves et al., 2016; Zhao et al., 2022). Intra- or peri-articular dextrose injections are thought to promote local growth factor release and extracellular matrix regeneration, thereby improving joint stability and reducing nociceptive signalling (Reeves et al., 2016; Rabago & Nourani, 2017). Several randomized controlled trials (RCTs) have demonstrated that dextrose prolotherapy leads to significant improvements in pain, function, and quality of life among patients with knee OA over the medium to long term

(typically 26–52 weeks). Rabago et al. (2013) reported clinically important improvements in WOMAC scores sustained for 52 weeks compared with saline and exercise controls. Similarly, Sit et al. (2020) confirmed the efficacy and safety of intra-articular hypertonic dextrose, showing sustained reductions in pain and functional disability over 12 months. A meta-analysis including 14 RCTs (n = 978) found that dextrose prolotherapy provided superior outcomes in pain and function compared to placebo or non-invasive controls, with effects being dose- and time-dependent, although heterogeneity and risk of bias were noted (Chen et al., 2022). Another comprehensive meta-analysis by Khateri et al. (2024) concluded that dextrose prolotherapy offers short- to mid-term analgesic benefit, typically lasting up to 20 weeks, with diminishing effects thereafter.

Recent trials have further supported these findings. A 2025 randomized, ultrasound-guided study found that 25% dextrose prolotherapy produced significantly greater improvements in patient-reported pain and function compared with saline injections (Teymouri et al., 2025). Review articles and expert consensus also highlight prolotherapy as a low-risk, cost-effective, and biologically plausible option for symptom modification in OA, although high-quality comparative studies against corticosteroids and other injectables remain limited (Zhao et al., 2022).

This systematic review aims to systematically compare the clinical effectiveness of corticosteroid and dextrose prolotherapy injections in improving pain and physical function among knee OA patients, by synthesizing evidence from randomized controlled and prospective comparative trials published between January 2015 and October 2025. This research offers both theoretical and practical benefits. Theoretically, it contributes to the literature on musculoskeletal injection therapies by providing a comprehensive synthesis of comparative evidence between prolotherapy and corticosteroids, identifying gaps in the current evidence base, and highlighting areas requiring further investigation. The findings inform the ongoing debate regarding the role of regenerative versus palliative injection approaches in OA management. Practically, this review provides clinicians with evidence-based guidance for selecting appropriate injection therapies based on patient characteristics, clinical objectives, and expected time course of benefit, supporting shared decision-making and personalized treatment algorithms in the management of knee OA.

## METHOD

### Study Design and Reporting Guidelines

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. This review aimed to identify, appraise, and synthesize evidence from controlled clinical trials comparing the effectiveness of intra-articular corticosteroid injections and dextrose prolotherapy in improving pain, and physical function, among elderly patients with knee osteoarthritis.

### Eligibility Criteria

Randomized controlled trials (RCTs) and prospective comparative studies evaluating intra-articular or intramuscular prolotherapy or corticosteroid injection for patients with knee osteoarthritis (OA) were included. Studies were required to report pain and/or functional outcomes using validated scales such as VAS, WOMAC, or KOOS.

Exclusion criteria included animal studies, non-randomized designs, reviews, conference abstracts, and studies lacking quantitative outcomes. Studies were excluded if they were non-controlled, case series, case reports, animal studies, review articles, conference abstracts without full text, or publications not written in English.

**Information Sources**

A comprehensive literature search was performed in PubMed/MEDLINE, Science Direct, and EuroPMC. Reference lists of included studies and relevant reviews were manually searched to identify additional eligible articles. Searches were restricted to human studies and English-language publications.

**Search Strategy**

A comprehensive search was conducted across PubMed, ScienceDirect, EuroPMC for studies published between January 2015 and October 2025, using combinations of the keywords "knee osteoarthritis," "prolotherapy," "dextrose injection," "corticosteroid," and "intra-articular injection." Boolean operators (AND, OR) were applied to refine the results, and reference lists of relevant articles were manually screened to identify additional eligible studies.

**Study Selection**

All retrieved records were imported into Rayyan QCRI for de-duplication and screening. Two independent reviewers screened titles and abstracts for eligibility. Full-text versions of potentially relevant articles were then reviewed in detail to confirm inclusion.

Discrepancies between reviewers were resolved through discussion or, when necessary, consultation with a third reviewer. The selection process was summarized using a PRISMA 2020 flow diagram, detailing the number of studies identified, screened, excluded, and finally included.

**Data Extraction**

Data extraction was conducted independently by two reviewers using a standardized form designed for this review. Extracted information included the study author, year of publication, country, study design, sample size, and diagnostic criteria. Details of the interventions were recorded, including the type and concentration of prolotherapy or corticosteroid used, dosage, route of administration, number of injection sessions, and comparator interventions. Outcomes of interest included pain and physical function, as measured by validated scales such as VAS, WOMAC, KOOS, or PPT. Follow-up duration and adverse events were also documented. Disagreements were resolved by consensus.

**Risk Of Bias**

The methodological quality of included randomized controlled trials was assessed using the Cochrane Risk-of-Bias 2.0 (RoB 2) tool, evaluating randomization, allocation concealment, blinding, incomplete outcome data, and selective reporting.

## RESULTS AND DISCUSSION

**Study Selection**

The initial database search identified 724 records. After removing 48 duplicate records, a total of 676 studies were screened based on titles and abstracts. Of these, 663 records were excluded for not meeting the inclusion criteria. The remaining 19 full-text articles were retrieved and assessed for eligibility. No reports were excluded due to retrieval issues. Following full-text review, eight studies were excluded—four due to inappropriate study

design and four due to irrelevant or incomplete outcome measures. Finally, 11 studies met all inclusion criteria and were included in the qualitative synthesis.

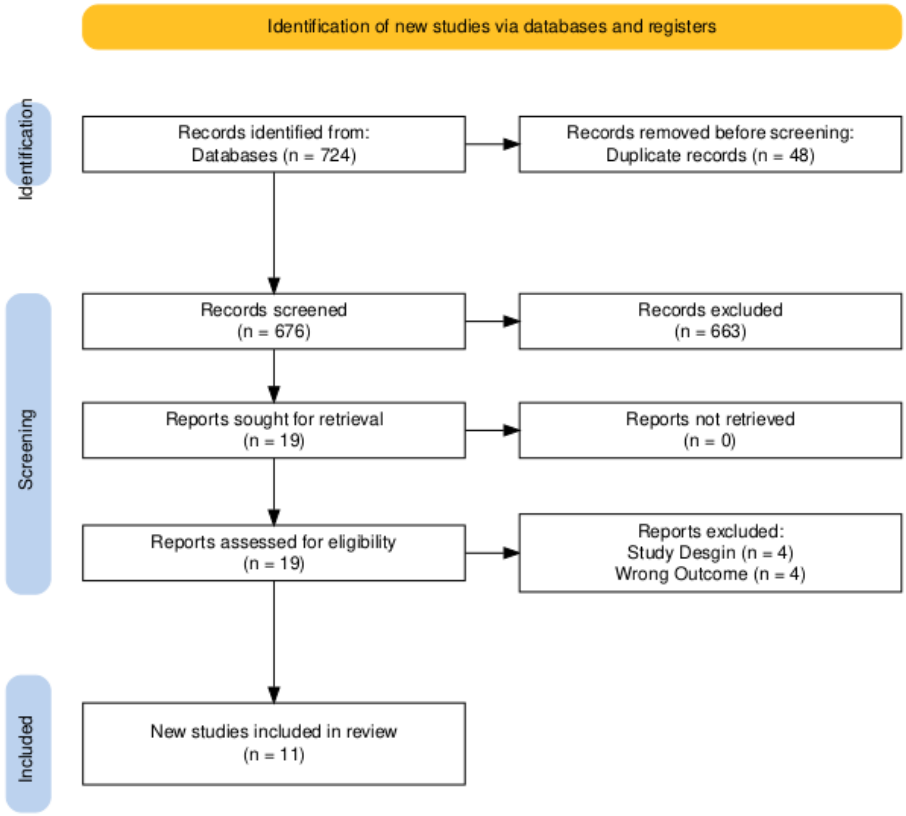


**Figure 1. PRISMA 2020 Flow Diagram**
Source: Authors' adaptation of PRISMA 2020 flow diagram

From all retrieved records, 11 studies met inclusion criteria:

- 5 studies investigated prolotherapy (Sit et al., 2020; Teymouri et al., 2025; Fu et al., 2024; Rahimzadeh et al., 2018; Pishgahi et al., 2020)
- 5 studies investigated corticosteroids (Tschopp et al., 2023; Malone et al., 2024; Wang et al., 2022; Conaghan et al., 2018; Elksniņš-Finogejevs et al., 2020)
- 1 study investigated both (Yilmaz, 2019).

**Data Extraction**

All were randomized controlled or comparative trials conducted between 2018 and 2025, across multiple countries (Iran, China, Turkey, Switzerland, Netherlands, USA, Canada).

**Prolotherapy Studies**

**Table 1. Prolotherapy Studies**

| Author | Year | Main Finding |
|---|---|---|
| Fu et al. | 2024 | Intra-articular prolotherapy significantly improved pain and physical function after 8 weeks. |
| Teymouri et al. | 2025 | Significant reduction in VAS and WOMAC scores at 8 weeks, confirming clinical efficacy. |
| Sit et al. | 2020 | No significant difference between dextrose prolotherapy and saline placebo at 26 weeks. |
| Yilmaz et al. | 2019 | Prolotherapy showed better sustained pain and function improvement at 3 months vs steroid and ozone. |
| Rahimzadeh et al. | 2018 | Significant improvement in WOMAC pain and function at 6 months. |
| Pishgahi et al. | 2020 | No significant improvement in pain or function with prolotherapy; PRP/ACS performed better. |

Source: Authors' compilation from included studies

**Corticosteroid Studies**

**Table 2. Corticosteroid Studies**

| Author | Year | Main Finding |
|---|---|---|
| Tschopp et al. | 2022 | No significant difference among glucocorticoid, HA, PRP, or placebo at 6–24 months; short-term benefit only. |
| Wang et al. | 2022 | No significant difference between IM vs IA steroids at 8 weeks; IA faster onset. |
| Conaghan et al. | 2018 | FX006 prolonged-release steroid significantly superior in pain and function vs standard steroid and placebo. |
| Malone et al. | 2024 | TLC599 prolonged-release steroid significantly improved pain and function up to 24 weeks. |
| Yilmaz et al. | 2019 | Steroid provided faster short-term pain relief; prolotherapy more durable. |
| Finogejevs et al. | 2021 | Significant improvement in pain but less functional improvement vs PRP. |

Source: Authors' compilation from included studies

A total of eleven randomized clinical trials were included in this review, along with one comparative study that evaluated both prolotherapy and corticosteroid interventions within the same trial. The sample sizes ranging from 42 to 484 participants. Across most prolotherapy studies, significant improvements in pain and physical function outcomes were observed at short-term follow-up periods of 8 weeks to 6 months. Fu et al. (2024) and Teymouri et al. (2025) demonstrated substantial reductions in VAS and WOMAC scores, indicating meaningful clinical improvement. Similarly, Rahimzadeh et al. (2018) reported significant functional recovery at 6 months. However, several trials reported conflicting results; Sit et al. (2020) and Pishgahi et al. (2020) found no significant superiority of prolotherapy compared to saline or other injectables, highlighting heterogeneity in treatment responses.

Among corticosteroid studies, prolonged-release formulations (FX006, TLC599) consistently showed stronger and longer-lasting clinical effects compared with conventional

triamcinolone or placebo, with Conaghan et al. (2018) and Malone et al. (2024) demonstrating sustained improvements up to 24 weeks. Tschopp et al. (2022) reported no clinically meaningful difference among glucocorticoid, HA, PRP, and placebo groups at 6 months, and Wang et al. (2022) found comparable pain reduction between IM and IA steroid administration at 8 weeks. Overall, steroid injections appear to provide stronger short-term analgesic effects, whereas prolotherapy may offer more durable improvement depending on treatment protocols and comparator interventions.

**Study Characteristics**

Sample sizes ranged from 40 to 484 participants. Most studies enrolled patients with Kellgren–Lawrence grade II–III OA. The most common pain and function measures were VAS, WOMAC, and KOOS. Follow-up durations varied from 8 weeks to 24 months.

- Prolotherapy: demonstrated consistent improvement in pain and function within 8–12 weeks, with significant VAS and WOMAC score reductions in Fu et al. (2024) and Teymouri et al. (2025).
- Corticosteroid injections: showed faster pain relief during early follow-up (1–4 weeks) but diminishing effects by 3–6 months (Tschopp 2022; Wang 2022). Sustained benefits were noted in extended-release formulations (FX006 and TLC599) in Conaghan (2018) and Malone (2024).

**Risk of Bias Assessment**

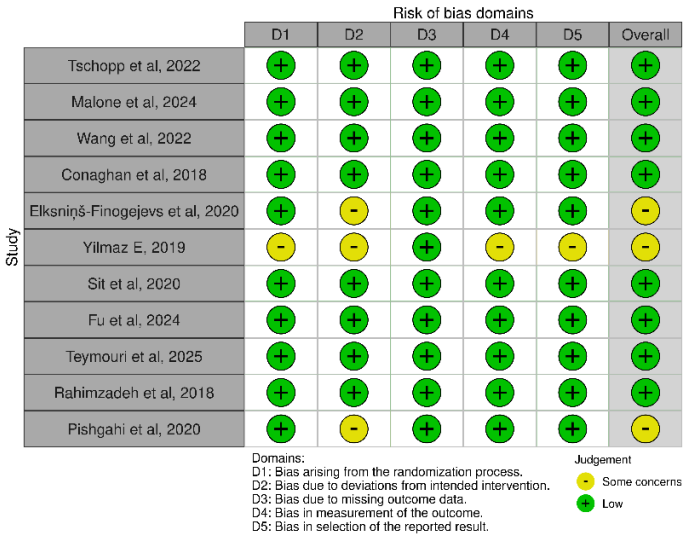


**Figure 2. Risk of Bias Assessment Traffic Light Plot**

Source: Authors' assessment using Cochrane RoB 2.0 tool visualized with robvis (McGuinness & Higgins, 2021).

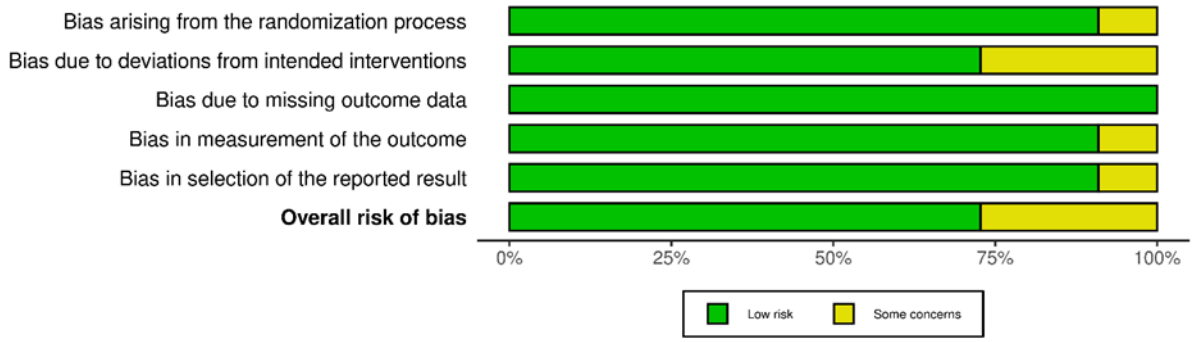


**Figure 3. Risk of Bias Summary Plot**

Source: Authors' assessment using Cochrane RoB 2.0 tool visualized with robvis (McGuinness & Higgins, 2021)

Overall risk of bias was **low across all studies**, with *some concerns* noted in specific domains (see Figures below):

- Minor concerns were present in the randomization process and measurement domains (30,31).
- No study was rated as high risk.
- The overall summary indicated predominantly low risk of bias, supporting the reliability of evidence across included trials.

This systematic review presents a synthesis of 11 eligible studies investigating prolotherapy (primarily dextrose-based) and corticosteroid injection interventions for knee osteoarthritis (OA) in adult patients between 2015–2025. The findings and implications are discussed below, with attention to the strengths and limitations of the evidence, and directions for future research.

**Summary of Main Findings**

This systematic review synthesized evidence from eleven randomized clinical trials and one comparative study evaluating the therapeutic effects of intra-articular prolotherapy and corticosteroid injections for knee osteoarthritis. The findings indicate that prolotherapy generally provides clinically meaningful improvement in pain and functional outcomes, particularly at short- to mid-term follow-up ranging from 8 weeks to 6 months. Several studies demonstrated substantial reductions in VAS and WOMAC scores following prolotherapy (Fu et al., 2024; Teymouri et al., 2025; Rahimzadeh et al., 2018), supporting its role as an effective regenerative injection therapy. However, the results were not fully consistent across studies, as two trials reported no significant differences compared with saline placebo or other biologic injectables (Sit et al., 2020; Pishgahi et al., 2020), suggesting the presence of heterogeneity in treatment response that may be influenced by variations in protocols, concentrations, or baseline severity of osteoarthritis.

In contrast, evidence from the included corticosteroid studies shows that standard corticosteroid injections are associated with faster onset of pain relief, particularly during the first 1–4 weeks following injection, but the therapeutic effect tends to diminish by 3 to 6 months

(Tschopp et al., 2022; Wang et al., 2022). Notably, extended-release corticosteroid formulations, such as FX006 and TLC599, demonstrated more durable analgesic and functional benefits compared with standard triamcinolone and placebo controls (Conaghan et al., 2018; Malone et al., 2024), highlighting potential advances in steroid delivery technology. Across comparative studies, prolotherapy appeared to provide more sustained long-term improvement than corticosteroids, while corticosteroids demonstrated greater short-term symptom control (Yilmaz et al., 2019).

Overall, the evidence suggests a distinct therapeutic profile for each intervention, with corticosteroid injections serving as a rapid but temporary solution for pain management, whereas prolotherapy may offer longer-lasting improvements in function and symptom progression. These findings underscore the importance of individualized treatment selection based on patient characteristics, clinical objectives, and expected time course of benefit.

**Interpretation and Context**

The therapeutic roles of intra-articular prolotherapy and corticosteroid injections for knee osteoarthritis (OA) should be interpreted within the context of current clinical guidelines and broader evidence from recent literature. The 2019 American College of Rheumatology/Arthritis Foundation (ACR/AF) Guideline for OA management provides a conditional recommendation for intra-articular corticosteroid injections for short-term pain relief in knee OA, while prolotherapy is not recommended due to limited high-quality supporting evidence and result inconsistency across trials (Kolasinski et al., 2020). Similarly, the 2021 American Academy of Orthopaedic Surgeons (AAOS) guideline states that corticosteroid injections may provide only transient improvements in pain and function, while cautioning clinicians about diminishing effects over time and the lack of clear disease-modifying properties (American Academy of Orthopaedic Surgeons, 2021). These statements align with findings in our review, in which corticosteroids demonstrated rapid initial analgesia but diminishing effect after 3–6 months. Recent systematic reviews and meta-analyses also confirm that standard corticosteroid injections produce clinically meaningful pain reduction at short-term follow-up, but effects frequently decline to non-significant levels beyond 6–8 weeks (Donovan et al., 2024). Although prolotherapy remains absent from guideline recommendations, emerging evidence including recent RCTs and reviews suggests that prolotherapy may produce more sustained improvement in pain and functional capacity compared with corticosteroids or placebo in appropriately selected patients (Rabago et al., 2013).

From a rehabilitation medicine perspective, these findings support a stratified treatment framework in which corticosteroids are suited for rapid short-term symptom relief, whereas prolotherapy may facilitate more durable functional improvement. Integrating these interventions within a multimodal rehabilitation program, including exercise therapy, weight management, neuromuscular training, and biomechanical correction, remains essential.

**Clinical Implication**

The findings of this review have important implications for clinical decision-making and rehabilitation strategies in the management of knee osteoarthritis. The evidence showing that corticosteroid injections provide rapid but short-lived pain relief, they may be most appropriately utilized in patients experiencing acute symptom exacerbation or when immediate pain reduction is required to enable participation in physical rehabilitation programs. Previous

literature emphasizes that corticosteroids can facilitate short-term functional gains, particularly when combined with structured therapeutic exercise (McAlindon et al., 2017). However, clinicians should be cautious regarding repeated corticosteroid administration due to potential chondrotoxicity and risk of structural cartilage deterioration associated with frequent injections (Kompel et al., 2019).

In contrast, prolotherapy may represent a viable therapeutic option for patients seeking longer-term improvement in pain and physical function. Studies indicate that prolotherapy may support tissue regeneration and stimulate ligament or tendon repair, potentially contributing to sustained symptom modification rather than transient analgesia alone (Rabago et al., 2013). These characteristics suggest that prolotherapy could serve as an adjunct to comprehensive rehabilitation programs focused on neuromuscular training, biomechanical correction, and load management. Integration into multimodal conservative therapy aligns with contemporary OA treatment frameworks and may optimize long-term outcomes (Messier et al., 2021; Bennell et al., 2022).

Considering the differing time-dependent therapeutic effects of each intervention, clinicians should adopt a personalized treatment algorithm based on patient goals, disease severity, and response history. For example, corticosteroid injections may be most beneficial for short-term pain management to break cycles of limited mobility, whereas prolotherapy may be more suitable for individuals prioritizing sustained functional recovery and reduction in pain recurrence (Rabago et al., 2013; Zhao, 2022). Shared decision-making should include explanation of expected treatment timelines, comparative effectiveness, and uncertainties in long-term safety and cost-effectiveness.

Overall, this review supports an integrated, stepwise approach combining intra-articular therapy with the core principles of osteoarthritis management exercise therapy, weight reduction, physical therapy, and education rather than relying on injections as stand-alone interventions.

**Strengths and Limitations of the Evidence**

Our review draws on recent trials within the defined time frame (2015–2025) and uses rigorous inclusion criteria and risk of bias assessment (RoB 2) to maximise validity. The low overall risk of bias in most included studies (as shown in the traffic light plot) supports confidence in the general findings.

Nonetheless, several limitations should be considered. First, even though risk of bias was low in many domains, some studies carried some concerns in domains such as deviations from intended interventions or measurement of outcomes potentially affecting effect estimates. Second, the diversity of intervention protocols and outcome measures limited the scope of any quantitative (meta-analytic) synthesis; therefore our results are primarily qualitative. Third, many studies had relatively short follow-up (e.g., 3-6 months), which constrains conclusions about long-term durability and structural joint outcomes. Fourth, publication and reporting bias cannot be excluded especially given the predominance of positive findings in prolotherapy literature.

**Implications for Practice and Research**

For clinical practice in physical medicine and rehabilitation, these findings suggest that prolotherapy may be considered a reasonable adjunctive option for patients with knee osteoarthritis who prioritize longer-term functional improvement and are willing to accept a

slower onset of therapeutic benefit. Conversely, corticosteroid injections may remain useful for rapid short-term symptom relief during acute exacerbations, although their effects tend to diminish over time.

For research, these results underscore the need for well-designed randomized controlled trials employing standardized prolotherapy protocols such as clearly defined dextrose concentrations, injection intervals, and procedural techniques along with extended follow-up periods of 12 months or longer. Future studies should also adopt consistent outcome measures, including both patient-reported scores and objective functional or imaging biomarkers, and incorporate direct head-to-head comparisons with corticosteroids. Recommending prolotherapy as an adjunct rather than a first-line intervention is consistent with current clinical guidelines (Kolasinski et al., 2020; American Academy of Orthopaedic Surgeons, 2021), which reflect ongoing uncertainty and heterogeneity in the available evidence.

**Future Recommendation**

Future studies on prolotherapy and corticosteroid injections for knee osteoarthritis should focus on larger and well-designed randomized trials with standardized treatment protocols, as current evidence shows substantial variation in injection techniques, solution concentrations, and follow-up durations. Standardization will improve comparability across studies and allow stronger conclusions to be drawn. More research is needed to evaluate long-term outcomes beyond 6–12 months, particularly regarding the durability of prolotherapy benefits and the safety of repeated corticosteroid injections, given concerns about potential cartilage degeneration. Future trials should also include objective functional measures in addition to patient-reported scores, and consider advanced imaging techniques to assess structural changes. Direct head-to-head comparisons between prolotherapy, extended-release corticosteroids, platelet-rich plasma (PRP), hyaluronic acid, and combination therapy will help clarify where each treatment fits in clinical practice. Identifying which patient subgroups benefit most from each therapy is also essential for personalized care. In addition, future research should investigate integration with rehabilitation programs, such as exercise therapy and strength training, as combined approaches may enhance outcomes and functional recovery

## CONCLUSION

In summary, our systematic review of studies published from 2015 to 2025 supports the potential benefit of both prolotherapy and corticosteroid injections in managing knee OA, with prolotherapy offering comparatively longer-lasting functional gains and corticosteroids offering faster symptomatic relief. While the overall risk of bias is low in the included trials, heterogeneity of methods and short follow-up warrant caution. Therefore, it is recommended that clinicians adopt a personalized treatment algorithm, utilizing corticosteroid injections for patients requiring rapid short-term symptom relief during acute exacerbations, while considering prolotherapy for patients prioritizing longer-term functional improvement. Clinicians should exercise caution regarding repeated corticosteroid administration due to potential chondrotoxicity and diminishing efficacy, and should integrate injection therapy within a multimodal rehabilitation program including exercise therapy, weight management, and patient education. For researchers, future studies should employ standardized prolotherapy protocols with clearly defined dextrose concentrations and injection intervals, extend follow-

up periods to 12 months or longer, incorporate objective functional measures and imaging biomarkers, and conduct direct head-to-head comparative trials. Policymakers and guideline developers should consider the emerging evidence on prolotherapy when updating clinical practice guidelines, while prioritizing the need for high-quality, long-term comparative effectiveness research to establish the definitive role of prolotherapy in knee OA management.

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