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Platelet-Rich Plasma Injections for Lower Back Pain

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Rapid Review

Table of Contents

Abbreviations	4
Key Messages	5
Context and Policy Issues	5
Research Question	6
Methods	6
Literature Search Methods	6
Selection Criteria and Methods	7
Exclusion Criteria.....	7
Critical Appraisal of Individual Studies	7
Summary of Evidence	7
Quantity of Research Available.....	7
Summary of Study Characteristics.....	8
Summary of Critical Appraisal.....	9
Summary of Findings	10
Limitations	12
Conclusions and Implications for Decision- or Policy-Making	13
References	14
Appendix 1: Selection of Included Studies	16
Appendix 2: Characteristics of Included Publications	17
Appendix 3: Critical Appraisal of Included Publications	19
Appendix 4: Main Study Findings	21
Appendix 5: Overlap Between Included Systematic Reviews	26
Appendix 6: References of Potential Interest	27

List of Tables

Table 1: Selection Criteria.....	7
Table 2: Characteristics of Included Systematic Reviews.....	17
Table 3: Strengths and Limitations of Systematic Reviews Using AMSTAR 2 ²⁰	19
Table 4: Summary of Findings by Outcome – Pain.....	21
Table 5: Summary of Findings by Outcome – Disability.....	23
Table 6: Summary of Findings by Outcome – Patient Satisfaction.....	24
Table 7: Summary of Findings by Outcome – Adverse Events.....	25
Table 8: Overlap in Relevant Primary Studies Between Included Systematic Reviews.....	26

List of Figures

Figure 1: Selection of Included Studies.....	16
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Abbreviations

CI	confidence interval
LBP	lower back pain
NRS	numerical rating scale
ODI	Oswestry Disability Index
OR	odds ratio
PRP	platelet-rich plasma
PRPIs	platelet-rich plasma injections
RCTs	randomized controlled trials
RR	risk ratio
SMD	standardized mean difference
VAS	visual analogue scale

Key Messages

- Platelet-rich plasma injections (PRPIs) might be better than other injections (including steroid injections) for patients with lower back pain in reducing pain and enhancing patient satisfaction, without increasing the risk of major complications or serious adverse events.
- For patients with low back pain who received PRPI, disability measures were lower up to 6 months after treatment than before PRPI, while MRI findings were unchanged from baseline.
- The included systematic reviews did not report any major complications or serious adverse events related to PRPIs.
- We did not find any studies reporting on the comparisons between PRPI and other conservative treatments such as non-steroidal anti-inflammatory drugs, exercise, or physiotherapy that met the inclusion criteria for this report.

Context and Policy Issues

Lower back pain (LBP) is a syndrome rather than a disease. LBP is characterized as pain in the region at the back of the body from the lower edge of the twelfth rib to the lower gluteal folds, with or without pain extending to 1 or both legs that persists for at least 1 day.¹ Chronic LBP refers to pain that persists for more than 12 weeks, even after receiving treatment for its potential causes.² LBP is a common and complex musculoskeletal problem and is the leading cause of disability or absence from work globally.^{1,3,4} People in all age groups, from children to older adults, can be affected by LBP. Approximately 60% to 80% of people experience LBP at some point during their lifetime.⁵ The point prevalence of activity-limiting LBP was about 7.3%, responsible for 60.1 million disability-adjusted life-years in 2015.⁴

The prevalence of LBP increases with age and peaks around 80 to 89 years.³ The age-adjusted prevalence of LBP was higher in females than males.³ Due to population increase and aging, LBP-induced years lived with disability, related costs, and health care use have increased substantially and will continue to increase in coming decades.⁴ Although most LBP episodes will recover within 4 to 6 weeks with little or no serious consequence,^{4,6,7} around 30% of people will suffer from at least 1 recurrent episode within 1 year after recovery.⁴ Similar epidemiology data and clinical features for LBP were reported in a Canadian national population health survey.⁶ In Canada, about 3% of people visited the emergency department with back pain from 2009 to 2015 in the largest emergency department in Atlantic Canada; among those with back pain, over 60% of patients were diagnosed with LBP.⁸

Only a small proportion of people with LBP had exact causes, such as vertebral fracture, infections, inflammatory disorders, or malignant disease.⁴ These types of disease-specific LBP need specific medical attention and management targeting the cause. However, most people with LBP cannot find the specific source of the pain. Multiple factors, including issues with intervertebral discs, facet joints, or vertebral end plates can cause nonspecific LBP.⁴ Lifestyle factors like smoking, obesity, and low levels of physical activity

may also contribute to this type of pain, as well as psychological factors and pain-processing mechanisms.⁴ Identifying the risk factors of LBP is important for treatment.

There are numerous treatment options available for LBP, including pharmacological and non-pharmacological therapies.⁹ Current guidelines suggest physical (mainly exercise), psychological interventions, and self-management strategies such as education, advice to remain active, or applying superficial heat, while these guidelines do not strongly emphasize surgery or injections.^{7,10} The effectiveness, safety, and cost-effectiveness are crucial considerations for choosing emerging interventions. Despite the emergence of injectable interventions for patients with LBP, they have not been widely implemented in clinical practice due to inconsistent or low-quality evidence regarding their clinical effectiveness and safety, and were not recommended by guidelines.^{7,10,11}

Platelet-rich plasma (PRP) is an injectable biologic product, which consists of a higher concentration of the patient's platelets in a small amount of plasma than in peripheral blood.¹² Clinicians have used PRP to treat various conditions for over 30 years,¹² including musculoskeletal disorders,¹³ surgical wounds,¹⁴ thin endometrium,¹⁵ premature ovarian failure,¹⁶ and acne scars.¹⁷ PRP contains numerous growth factors in platelet granularities such as fibroblast growth factor, transforming growth factors beta-1, angiogenesis factor, and growth factor.¹² The exact mechanisms by which PRP and its components can treat these diseases are not yet clear, but they might be involved in tissue repair, pain relief, and regenerative processes.¹³⁻¹⁷

PRPIs are becoming 1 potential intervention for patients with LBP.¹⁸ Based on a nonsystematic literature review,¹⁹ several observational studies have reported the effectiveness of PRPIs; however, there is lack of high-quality clinical trials in this population. Given the uncertain and developing evidence base for PRPIs, the objective of this report is to evaluate the recent evidence on the clinical effectiveness and safety of PRPIs for the treatment of LBP in adults.

Research Question

What is the clinical effectiveness of platelet-rich plasma injections for the treatment of lower back pain in adults?

Methods

Literature Search Methods

An information specialist conducted a literature search on key resources, including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, and a focused internet search. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevancy. The search strategy comprised controlled vocabulary, such as the National Library of Medicine's MeSH (Medical

Subject Headings), and keywords. Search concepts were developed based on the elements of the research questions and selection criteria. The main search concepts were platelet-rich plasma injections and back pain. Conference abstracts were excluded. Retrieval was limited to the human population. The search was completed on April 27, 2023 and limited to English-language documents published since January 1, 2018.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first screening level, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in [Table 1](#). For this report, we considered a review to be a systematic review if it indicated that the evidence was searched for systematically and had clear inclusion and exclusion criteria.

Table 1: Selection Criteria

Criteria	Description
Population	Adults with lower back pain
Intervention	Platelet-rich plasma injections
Comparator	Usual care (e.g., no treatment with platelet-rich plasma injections, exercise or physiotherapy, cortisone injections, non-steroidal anti-inflammatory drugs)
Outcomes	Clinical benefits (e.g., pain, function, mobility, quality of life, patient satisfaction) and harms (e.g., adverse events)
Study designs	Health technology assessments and systematic reviews

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in [Table 1](#), they were duplicate publications, or were published before 2018. Systematic reviews and health technology assessments in which all relevant primary studies were captured in at least 1 other more recent or more comprehensive systematic review were excluded.

Critical Appraisal of Individual Studies

The included systematic reviews were critically appraised by 1 reviewer using A MeaSurement Tool to Assess systematic Reviews 2 (AMSTAR 2).²⁰ Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 123 citations were identified in the literature search. Following screening of titles and abstracts, 90 citations were excluded and 33 potentially relevant reports from the electronic search were retrieved for full-text review. Ten potentially relevant publications were retrieved from the grey literature search for

full-text review. Of these potentially relevant articles, 39 publications were excluded for various reasons, and 4 systematic reviews met the inclusion criteria and were included in this report. [Appendix 1](#) presents the PRISMA²¹ flow chart of the study selection.

Additional references of potential interest are provided in [Appendix 6](#).

Summary of Study Characteristics

We included 4 systematic reviews in this report.²²⁻²⁵ Two^{23,25} of the 4 systematic reviews had broader inclusion criteria on interventions than the present report. Specifically, both systematic reviews^{23,25} included both PRPIs and mesenchymal stem cell interventions. Only the subset of studies reporting on PRPIs was relevant to this rapid review and are described in the remainder of our report. Additional details regarding the characteristics of included publications are provided in [Appendix 2](#).

[Appendix 5](#) includes a table describing the overlap in relevant primary studies in the included systematic reviews.

Study Design

Two^{22,25} of 4 systematic reviews included single-arm meta-analyses comparing the outcome after treatment to baseline, 1 systematic review²⁴ included the meta-analyses comparing PRPIs to control interventions, and 1 systematic review²³ summarized the findings from primary studies narratively and did not conduct a meta-analysis. The number of primary studies involving PRPIs that were included in the systematic reviews ranged from 3 to 15 primary studies,^{22,25} which comprised randomized controlled trials (RCTs), observational studies, and case reports. One systematic review²⁵ was published in 2018, 1 systematic review²⁴ was published in 2020, 1 systematic review²³ was published in 2022 and 1 systematic review²² was published in 2023 with the search up to April 18, 2022. We found 1 systematic review²⁴ that consisted of 3 RCTs, which were also included in another systematic review.²⁵ We utilized both systematic reviews^{24,25} because the former compared PRPI interventions to control interventions in their meta-analyses,²⁴ while the latter had a wider range of studies but only conducted single-arm meta-analyses.²⁵

Country of Origin

Of the 4 systematic reviews, 2 systematic reviews^{22,24} were from China, 1 systematic review was from Italy,²³ and 1 systematic review was from the US.²⁵ One systematic review²² presented the countries or regions of included primary studies. Of the 6 studies within this systematic review, 3 RCTs were conducted in the US and 3 observational studies were conducted in Japan, India, and the US.²²

Patient Population

Two^{22,23} of 4 systematic reviews²²⁻²⁵ involved patients with chronic discogenic LBP. One review included patients with LBP but did not report the type or duration of LBP.²⁴ One review included patients with LBP and lower extremity pain (duration not reported).²⁵ The number of included patients in 3 systematic reviews²²⁻²⁴ ranged from 127 to 198. The mean age of patients in primary studies within 2 systematic reviews^{22,24} ranged from 33 years to 52.91 years and age was not reported in the 2 remaining systematic reviews.^{23,25} In 2

systematic reviews, the percentage of males ranged from 39% to 80%^{22,24} and was not reported in the other 2 systematic reviews.^{23,25}

Interventions and Comparators

One systematic review²⁴ compared the effectiveness and safety of PRPIs to control injections without PRPIs, which included anesthetic, steroids, or contrast agents. The remaining 3 systematic reviews^{22,23,25} reported the before and after changes for receiving PRPIs without a comparator group. PRPI sites or routes of administration were reported as intradiscal,^{22,25} sacroiliac joint,^{24,25} intra-articular,^{24,25} and epidural injection.²⁵ One systematic review²³ did not report the site of the injection for PRP, but reported the injected PRP volumes ranged from 1 mL to 3 mL, when reported.^{23,24} None of the systematic reviews²²⁻²⁵ clearly reported the types of PRP used (pure or leucocyte PRP), the frequencies of the injections, treatment history, and the co-interventions for LBP.

Outcomes

All 4 systematic reviews reported or discussed pain outcomes.²²⁻²⁵ Pain was assessed by the visual analogue scale (VAS) or numerical rating scale (NRS). In 2 systematic reviews,^{22,24} the VAS or NRS were reported in a 10-point scale, while the scale of pain measures was clear in the other 2 systematic reviews.^{23,25} The disability was assessed in 2 systematic reviews^{22,25} by Oswestry Disability Index (ODI),²² Functional Rating Index, or Roland-Morris Disability Questionnaire.²⁵ The pain or disability scales used in individual studies were not reported in detail, including their psychometric properties and interpretation scores such as what direction represents improvement or worsening, or minimal important difference. Three systematic reviews²²⁻²⁴ mentioned adverse events or major complications. One systematic review²³ described the MRI changes after PRPIs treatment. One systematic review²⁴ also reported the rate of patient satisfaction. Three systematic reviews reported the mean or median duration of follow-up,²²⁻²⁴ which ranged from 1 week to 60 weeks. The remaining systematic review did not report the duration of follow-up.²⁵

Summary of Critical Appraisal

In all 4 systematic reviews,²²⁻²⁵ the objective was clearly described, multiple databases were searched, keywords or medical subject terms or keywords of the search and study selection flow charts were provided, the review authors declared no conflicts of interest, lists of included articles were presented and the study characteristics were described. None of the systematic reviews provided lists of excluded articles or assessed the sources of funding in individual studies. Despite searching in multiple databases, 3 systematic reviews²²⁻²⁴ did not report performing a grey literature search and 2 systematic reviews^{23,25} did not report searching the Embase database specifically. These limitations may result in missing some studies (unpublished or studies conducted in Europe) or mis-identification of potential publication bias.

At least 2 reviewers independently performed the article selection and data extraction in 1 systematic review.²³ Two reviewers independently selected articles in 2 systematic reviews,^{22,25} but it was unclear how the data extraction was performed. In the fourth systematic review,²⁴ it was unclear how article selection and data extraction were conducted. The possibility of inappropriate inclusion or exclusion or errors in data extraction cannot be ruled out. Although 3 systematic reviews²²⁻²⁴ assessed the risk of bias of included

individual studies and reported study quality, they did not assess the potential impact of study risk of bias on the interpretation of results. One systematic review²³ authors judged that only 1 out of 7 primary studies had high-quality (low risk of bias); in another systematic review²², some meta-analyses only included 1 or 2 primary observational studies; therefore, the results of these analyses may be driven by individual studies with high risk of bias. One systematic review²⁵ evaluated the grading of evidence, considering the quality of included individual studies and stratified the assessment according to PRPI sites. However, the review²⁵ did not include an outcome-specific assessment of evidence, making it challenging to interpret the reported level of evidence. In 2 systematic reviews^{22,25} with substantial statistical heterogeneity, no analysis was conducted to explore the observed heterogeneity.

The systematic review by Peng et al. (2023)²² included a single-arm meta-analysis to compare the changes in pain and disability outcomes between post-PRPI treatment and baseline and calculated incidence rates for improvement; this analysis was methodologically flawed. The review authors²² calculated the incidence rate for improvement in outcome measures of over 30% or 50% based on the pooled odds ratio (OR) in their meta-analysis. The formula used to calculate the incidence rate was “incidence rate = $OR / (1 + OR)$ ” and the results were reported as percentages. To accurately calculate the incidence rate, 1 must consider the new events, the population at risk, and a time frame, and report it as events per people-year. Reporting the incidence rate results based on a pooled OR is unreliable. Alternatively, the systematic review authors could have extracted the proportion of patients who experienced a 30% or 50% decrease in pain or disability and use appropriate proportional meta-analysis to get a pooled proportion.²⁶

Additional details regarding the strengths and limitations of included publications are provided in [Appendix 3](#).

Summary of Findings

One included systematic review²⁴ compared PRPIs and controls interventions without PRPIs. Two systematic reviews^{22,25} included data from RCTs or observational studies on patients who received PRPI and conducted meta-analyses of data from the intervention arm alone. The fourth systematic review²³ provided narrative summaries of the findings of the individual studies that were included (1 out of 7 included individual studies had a control group and the details of control were unclear). [Appendix 4](#) presents the main study findings. Due to some overlap in the studies included in the 2 systematic reviews with single-arm meta-analyses^{22,25} the pooled estimates from the 2 systematic reviews may contain some of the same individual study data ([Appendix 5](#)).

Clinical Effectiveness of PRPI

Pain Scores

All included systematic reviews²²⁻²⁵ reported pain scores after PRPI in people with LBP, and generally demonstrated statistically significant reductions from baseline or compared to a control. One systematic review²⁴ reported that PRPI was statistically significantly more effective than the control group in reducing pain scores within 8 weeks. However, the method of measurement for the pain scores was unclear. Two systematic reviews^{22,25} reported the pooled estimates of post-PRPI pain scores at various time points from single-arm meta-analysis. These systematic reviews reported that pain scores were statistically reduced at

1 month,²² 2 months,²² 6 months,^{22,25} and 12 months²⁵ after PRPI compared with before PRPI with substantial statistical heterogeneity ($I^2 = 77\%$ to 98%). However, the comparisons of pain scores between post-PRPI time points were not statistically significant.²² For PRP administered by lumbar facet joint injection, intra-articular injection and sacroiliac joint injection, the systematic review by Sanapati et al. (2018)²⁵ provided a narrative summary of findings for each study in tables, indicating that most studies reported positive effects of PRPI on pain (i.e., pain decreased). One systematic review²³ reported the findings from 4 primary studies in which pain scores were numerically lower after PRPI treatment (unclear time point) compared with before PRPI treatment. However, it is unclear what methods were used to measure pain scores and the time frame for outcome measures.

The systematic review by Sanapati et al. (2018)²⁵ also reported the level of evidence, but failed to specify it based on the outcomes (pain or disability). PRP treatment administered through lumbar disc injection has a level III (fair) evidence in reducing pain.²⁵ However, for lumbar facet joint, intra-articular injection, and sacroiliac joint injection, the level of evidence was level IV (limited).²⁵ In this review,²⁵ level III (fair) evidence was defined as “evidence obtained from at least one relevant high quality nonrandomized trial or observational study with multiple moderate or low-quality observational studies” and level IV (limited) was defined as “evidence obtained from multiple moderate or low-quality relevant observational studies” (page 519, Table 1).

Number of Patients With Pain Relief

One systematic review²⁴ reported that PRPI was statistically significantly more effective than the control group in improving the rate of patients who experienced at least 50% pain relief at 3 months. Another systematic review²² reported the calculated incidence rates based on pooled odds ratios for patients who experienced more than 30% and 50% pain relief after PRPI treatment compared with before PRPI treatment at 1 month, 2 months, and 6 months, with more than half of patients reaching at least 30% of pain relief at any measured time points. However, the reliability of these incidence rates is questioned due to the use of flawed methods or formulas.

Disability

Two systematic reviews^{22,25} reported disability outcomes. One systematic review²² evaluated the incidence rates of patients who experienced a 30% or 50% decrease from baseline in disability score after PRPI treatment. This review reported 40.2% of patients reaching at least a 30% decrease in disability score at 2 months, and 53.9% reaching at least a 50% decrease in disability score at 6 months. However, we had concerns regarding the accuracy of the findings due to the utilization of incorrect methods or formulas in this review. The second review²⁵ reported that the disability scores were numerically lower after PRPI treatment at 3 months or 6 months than before PRPI treatment.

Patient Satisfaction

One systematic review reported that PRPI can statistically significantly enhance patient satisfaction rates compared to control interventions.²⁴ The details of the outcome measure, such as the time it was taken, the tool used to assess patient satisfaction and its psychometric properties, and whether the outcome assessors were blinded to group allocation, were not provided.

Adverse Events

All 4 systematic reviews²²⁻²⁵ considered adverse events, and 1 review²⁴ provided a meta-analysis on adverse events. Based on the meta-analysis,²⁴ there was no statistical difference in adverse events between patients in the PRPI treatment group and the control group. Two systematic reviews reported that no serious adverse events or complications occurred.^{22,23} In the fourth systematic review,²⁵ adverse events were considered for some individual studies in tables, and PRPIs did not appear to have serious safety concerns. However, the definitions of considered adverse events were not provided.

Other Outcomes

One systematic review based on 2 individual studies noted that, for most patients, there were no significant changes in hydration level, height of the intervertebral disc, and disc bulging in MRI after PRPI intervention compared to before PRPI intervention.²³

Limitations

There are some methodological limitations in the body of evidence presented. In this report, we identified 4 systematic reviews²²⁻²⁵ to answer the research question on clinical effectiveness of PRPIs. Two^{22,25} of these reviews used single-arm meta-analysis to provide before-after comparisons of outcomes in within the PRPI group, while 1 systematic review²³ narratively summarized the findings of the included primary studies. Only 1 systematic review²⁴ included a meta-analysis comparing PRPI to the control group. Most of the primary studies included in these reviews were observational studies, with only a small number of RCTs (3 RCTs per systematic review in 2 systematic reviews^{22,24}). The sample sizes of included systematic reviews²²⁻²⁴ were relatively small, with fewer than 200 patients. For the results from before-after comparison, observational studies or RCTs with high risk of bias, we cannot conclusively determine that the changes in the outcome measure are solely caused by the PRPI intervention, and there may be potential selection bias, recall bias, or performance bias. None of the systematic reviews conducted subgroup analysis or meta-regression to investigate the observed statistical heterogeneity. Moreover, 1 systematic review²² employed flawed methods to calculate the incidence rate.

The body of evidence also has issues with unclear reporting. All included systematic reviews²²⁻²⁵ did not provide a comprehensive description of the types of PRPI used such as pure or leucocyte PRP or the frequencies of the injections. In addition, the treatment history or co-interventions with the PRPIs intervention were not clearly provided. We are unclear about the psychometric properties for disability measures, the definition of the patient satisfaction and adverse events. Thus, the interpretations of evidence regarding these outcomes were limited.

We also noted some evidence gaps in this report. There was no systematic review conducted that considered the patients' perspective by comparing the observed mean difference with the tool's minimal important difference in their statistical findings. Moreover, no systematic review was found that reported the comparisons between PRPI and other conservative treatments such as non-steroidal anti-inflammatory drugs, exercise or physiotherapy in the current report. The primary studies of 1 included systematic review²²

were conducted in Asia and the US. Thus, the generalizability of these findings to settings in Canada is uncertain.

Conclusions and Implications for Decision- or Policy-Making

Four systematic reviews²²⁻²⁵ were identified to address the clinical effectiveness of PRPI for patients with LBP. These studies provided evidence from RCTs, before and after studies, and case reports to suggest that patients with LBP treated with PRPI had statistically significantly reduced pain (up to 12 months) or disability scores (up to 6 months) compared to before PRPI treatment. One systematic review²⁴ that included 3 RCTs reported that PRPI may be better than control injections (including steroid injections) for patients with LBP in reducing pain scores within 8 weeks, improving the number of patients who experienced at least 50% pain relief at 3 months, and enhancing patient satisfaction, without increasing the adverse event rate. No major complications or adverse effects related to PRPIs were reported in all included systematic reviews.²²⁻²⁵ Due to the potential bias of observational studies and before-after designs, these findings need to be interpreted with caution.

Individuals with LBP typically require a range of interventions, both pharmacological and non-pharmacological interventions.⁹ One systematic review²³ only included patients who did not respond to conservative treatment and had MRI evidence of disc degeneration. Other included systematic reviews^{22,24,25} did not clearly report the indication for starting PRPI treatment. Additionally, the definition of conservative treatment was unclear, leaving uncertainty about whether all individuals need an MRI or conservative treatment before further intervention with PRPI.

The prognosis of patients with LBP is relatively good in that most patients can recover with other treatment such as exercise or physiotherapy;^{4,6,7,9} however, we did not identify any studies comparing PRPI with exercise or physiotherapy that met our inclusion criteria. We may need such comparative studies to fully assess the benefits of adding PRPI to usual care or other interventions. When there is acceptable variability in population and intervention characteristics, conducting a systematic review with network meta-analysis may be helpful to get the relative effect of PRPI versus other active interventions. Considering the current limitations of the body of evidence, primary studies with robust design and adequate sample size that address the relative effects of PRPI versus other treatments are also needed. The accessibility and cost of PRPI, and the values or preferences of patients regarding injections can also play a significant role in the decision-making process.

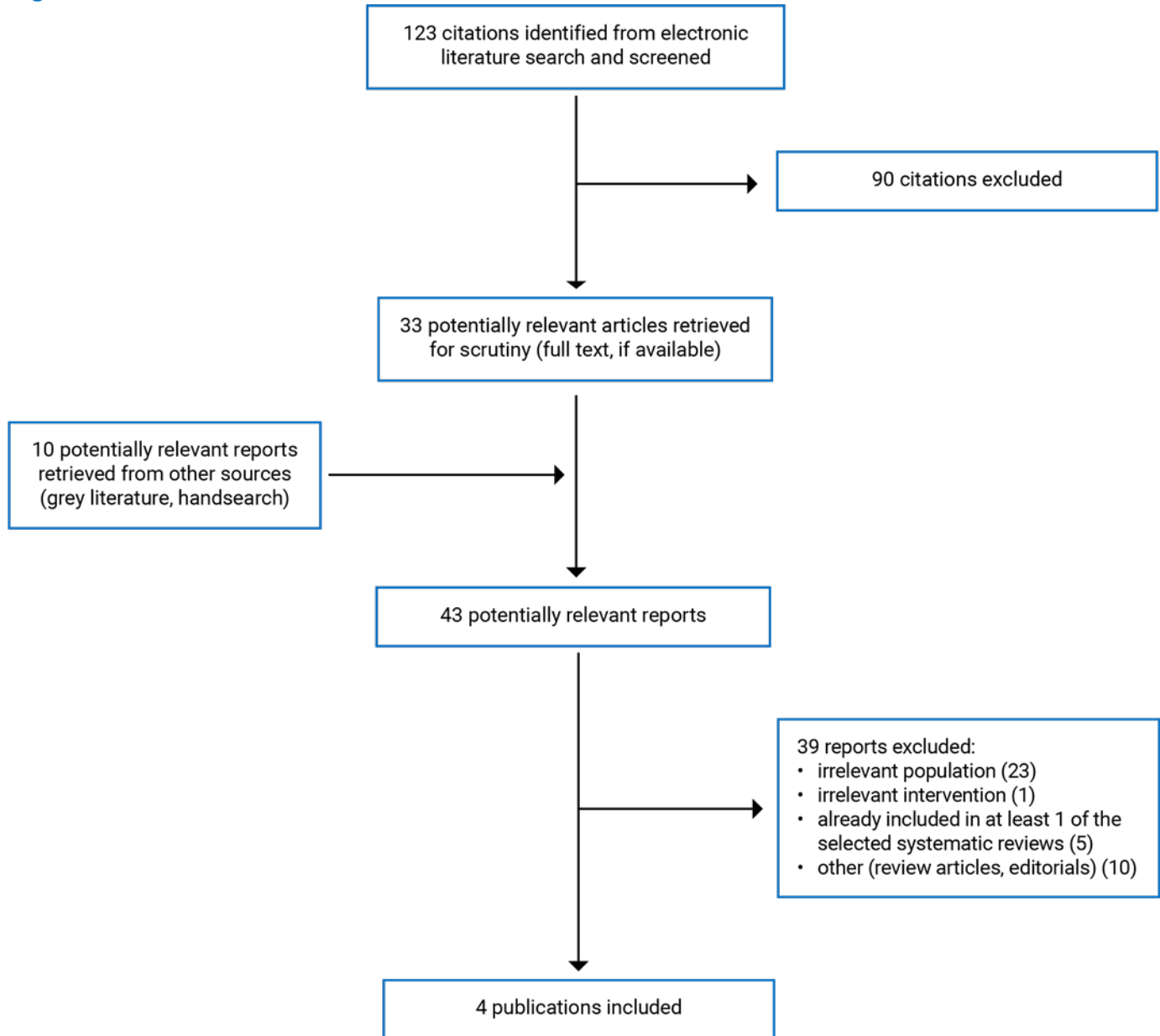
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Appendix 1: Selection of Included Studies

Figure 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Note that this appendix has not been copy-edited.

Table 2: Characteristics of Included Systematic Reviews

Study citation, country, funding source	Study designs and numbers of primary studies included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Peng et al. (2023) ²² China Funding source: National Natural Science Foundation of China and Changsha City	Study design: systematic review with single-arm meta-analysis Number of included and relevant studies: 6	Patients with discogenic LBP Number of patients: 127 (number in the individual studies ranged from 14 to 29) Sex: male (n = 8 to 14, 45% to 60%) Mean age: from 33 to 47.5 years. Disease duration: one study reported a median of 90 days; for other studies over 3 or 6 months.	Intervention: intradiscal injection of PRP Comparator: Baseline scores in the same group	Outcomes: <ul style="list-style-type: none"> • Pain (VAS or NRS scale, 10-point) • ODI scores • Adverse events Follow-up: from 1 week to 60 weeks
DI Martino et al. (2022) ²³ Italy Funding source: the authors declared no conflict of interest.	Study design: systematic review of RCTs, observational studies, and/or case reports without meta-analysis Number of included studies: 17 (7 were relevant to the current report).	Patients with discogenic LBP, failure of conservative treatment, MRI evidence of disc degeneration Number of patients: 198 Sex: NR Mean age: NR Disease duration: at least 3 to 6 months	Intervention: Autologous PRP (volume injected between 1 mL and 3 mL). Comparator: 1 individual study had a control group without comparator details and for other studies, the comparator was baseline score in the same group	Outcomes: <ul style="list-style-type: none"> • Pain VAS • MRI changes • Major complications or adverse effects Follow-up: from 2 months to 12 months
Xuan et al. (2020) ²⁴ China Funding source: the authors declared no conflict of interest.	Study design: systematic review of RCTs Number of included and relevant studies: 3	Patients with LBP Number of patients: 131 (number in the individual studies ranged from 40 to 46) Sex: males in the intervention group: n = 10 to 16, proportion = 43% to 80%; in the control group: n = 9 to 16, proportion = 39% to 80%.	Intervention: intra-articular injection with PRP; Ultrasound-guided sacroiliac joint injection with 3 mL leukocyte-free PRP with 0.5 mL calcium chloride; Intradiscal injection. Comparator: Intra-articular injection with local anesthetic/corticosteroid; ultrasound-guided	Outcomes: <ul style="list-style-type: none"> • Pain (VAS or NRS scale, 10-point) • Patient satisfaction • Adverse events Follow-up: from within 8 weeks to 1 year

Study citation, country, funding source	Study designs and numbers of primary studies included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
		Mean age: from 35 to 52.91 years Disease duration: NR	sacroiliac joint injection with 1.5 mL methylprednisolone (40 mg/mL); Intradiscal contrast drug.	
Sanapati et al. (2018) ²⁵ US Funding source: the authors declared no conflict of interest.	Study design: systematic review of RCTs, observational studies and case reports with single-arm meta-analysis Number of included studies: 21 (15 were relevant to the current report).	Patients with LBP and lower extremity pain Number of patients: NR Sex: NR Mean age: NR Disease duration: NR	Intervention: PRP (lumbar disc injections, epidural injections, lumbar facet intra-articular injections, sacroiliac joint injection) Comparator: Baseline scores in the same group	Outcomes: <ul style="list-style-type: none"> • Pain score • Disability measures: Functional rating index, Roland-Morris Disability Questionnaire Follow-up: NR

NA = not applicable; NR = not reported; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire; NRS = Numerical Rating Scale; RCTs = randomized controlled trials; PRP = platelet-rich plasma; LBP = lower back pain; VAS = visual analogue scale.

Appendix 3: Critical Appraisal of Included Publications

Note that this appendix has not been copy-edited.

Table 3: Strengths and Limitations of Systematic Reviews Using AMSTAR 2²⁰

Strengths	Limitations
Peng et al. (2023)²²	
<p>The purpose of the study was clearly described.</p> <p>The intervention, comparator, and study designs of the individual study for inclusion were clearly described.</p> <p>The protocol of this review was prospectively registered in the INPLASY (202240108).</p> <p>Multiple databases were searched (PubMed, Embase, Cochrane Library, Clinical Trials databases and Chinese databases).</p> <p>Medical subject terms, related entry terms, and search strategy for PubMed were provided.</p> <p>The authors manually searched reference lists of retrieved studies and related reviews.</p> <p>A flow chart of study selection was provided.</p> <p>The details of included studies were described.</p> <p>The review authors assessed risk of bias for included RCTs using Cochrane Risk of Bias Assessment Tool and for included observational studies using the Newcastle–Ottawa Scale.</p> <p>The full-text screening and risk of bias assessments were clearly described and conducted by 2 reviewers independently.</p> <p>The review authors declared no conflicts of interest.</p>	<p>A grey literature search was not reported.</p> <p>The list of excluded studies was not provided.</p> <p>The review authors did not report the funding sources for eligible studies.</p> <p>It is unclear if the study data extractions were performed by 2 authors independently.</p> <p>The review authors did not assess the potential impact of risk of bias in individual studies on result interpretations.</p> <p>The review authors used the wrong formula, incidence rate = OR/ (1+OR), to calculate the incidence rate and related confidence intervals for improvement in outcome measures.</p> <p>The review authors use inappropriate methods for the statistical combination of results.</p> <p>No explanation provided for the observed heterogeneity in the results.</p> <p>Publication bias was not assessed.</p> <p>Sensitivity analyses were not conducted.</p>
DI Martino et al. (2022)²³	
<p>The purpose of the study was clearly described.</p> <p>Multiple databases were searched (PubMed, Medscape, MEDLINE, Google Scholar, and Cochrane databases).</p> <p>Keywords used in the search were provided.</p> <p>References from the identified articles were checked.</p> <p>A flow chart of study selection was provided.</p> <p>The review authors assessed the risk of bias in included studies using the quality index checklist developed by Downs and Black.</p> <p>The study selection processes were clearly described and conducted by 2 reviewers.</p> <p>The data extraction process was prepared and agreed upon by 3 independent authors.</p> <p>The review authors declared no conflicts of interest.</p>	<p>The outcomes and study designs of the individual study were not clearly described.</p> <p>Embase was not searched.</p> <p>The full search strategy was not available.</p> <p>A grey literature search was not reported.</p> <p>The review authors did not assess the risk of bias for eligible studies and potential publication bias.</p> <p>The list of excluded studies was not provided.</p> <p>The review authors did not report the funding sources for eligible studies.</p> <p>The review authors did not assess the potential impact of risk of bias in individual studies on result interpretations.</p>
Xuan et al. (2020)²⁴	
<p>The purpose of the study was clearly described.</p> <p>The study designs of the individual study for inclusion were clearly described.</p>	<p>The diagnostic criteria of LBP, disease durations, and background therapies were not clearly described.</p> <p>A grey literature search was not reported.</p>

Strengths	Limitations
<p>Multiple databases were searched (PubMed, Embase, Web of Science, EBSCO, and the Cochrane Library).</p> <p>Keywords in the search were provided.</p> <p>The authors hand-searched the reference lists of the retrieved studies and the relevant reviews.</p> <p>A flow chart of study selection was provided.</p> <p>The details of included studies in were adequately described.</p> <p>The review authors assessed the risk of bias for eligible studies using the Jadad scale.</p> <p>The review authors use appropriate methods for the statistical combination of results.</p> <p>The review authors declared no conflicts of interest.</p>	<p>We are unclear if the study selection process, the data extractions, and risk of bias assessments were performed by 2 authors independently.</p> <p>The list of excluded studies was not provided.</p> <p>The reported figures and main text showed inconsistencies in the direction of the treatment effect on pain relief at 3 months and patient satisfaction.</p> <p>The review authors did not report the funding sources for eligible studies.</p>
<p>Sanapati et al. (2018)²⁵</p>	
<p>The purpose of the study was clearly described.</p> <p>Multiple databases were searched (PubMed, Cochrane library, US National Guideline Clearing house, and Clinical trials).</p> <p>The authors also searched the references of the previous systematic reviews and cross references, and other sources such as non-indexed journals and abstracts.</p> <p>The search strategy was provided.</p> <p>A flow chart of study selection was provided.</p> <p>The full-text screening and risk of bias assessments were clearly described and conducted by 2 reviewers independently.</p> <p>The review authors assessed the risk of bias for eligible studies using multiple tools, including the Cochrane review rating system, Interventional Pain Management Techniques -- Quality Appraisal of Reliability and Risk of Bias Assessment Tool for RCTs and observational studies.</p> <p>The authors provided the level of evidence according to the best-evidence synthesis and multiple available criteria, including the Cochrane Review criteria and the United States Preventive Task Force criteria.</p> <p>The review authors declared no conflicts of interest.</p>	<p>The intervention and outcome measures of the individual study were not clearly described.</p> <p>Embase was not searched.</p> <p>It is unclear if the study data extractions were performed by 2 authors independently.</p> <p>The review authors did not assess potential publication bias.</p> <p>The list of excluded studies was not provided.</p> <p>The review authors did not report the funding sources for eligible studies.</p> <p>The confidence interval stated in the main text regarding the mean difference in pain scores from baseline to the 12-month follow-up does not match the figures presented in the related Figure 3.</p> <p>No analysis was conducted to explore the observed statistical heterogeneity.</p>

AMSTAR 2 = A Measurement Tool to Assess systematic Reviews 2; NA = not applicable; NR = not reported; OR = odds ratio; RCTs = randomized controlled trials.

Appendix 4: Main Study Findings

Note that this appendix has not been copy-edited.

Table 4: Summary of Findings by Outcome – Pain

Author (year) and study design	Results					
	Time points	Statistics	Effect size	Method of measurement	P	Notes
Pain scores						
Peng et al. (2023) ²² Systematic review with 6 articles: 3 RCTs and 3 perspective cohort studies	1 month	Pooled SMD (95% CI)	-1.04 (-1.89 to -0.20)	VAS or NRS with 10-point scale	0.02	Before-after intradiscal PRPI, from meta-analysis with 3 studies
	2 months	Pooled SMD (95% CI)	-1.33 (-2.20 to -0.46)	VAS or NRS with 10-point scale	0.003	Before-after intradiscal PRPI, from meta-analysis with 3 studies
	6 months	Pooled SMD (95% CI)	-1.42 (-2.25 to -0.59)	VAS or NRS with 10-point scale	0.0008	Before-after intradiscal PRPI, from meta-analysis with 4 studies
	1 month vs. 2 months	Pooled SMD (95% CI)	-0.20 (0.55 to 0.14)	VAS or NRS with 10-point scale	0.25	Unclear methods
	1 month vs. 6 months	Pooled SMD (95% CI)	-0.13 (-0.48 to 0.21)	VAS or NRS with 10-point scale	0.45	Unclear methods
	2 months vs. 6 months	Pooled SMD (95% CI)	0.06 (-0.28 to 0.41)	VAS or NRS with 10-point scale	0.72	Unclear methods
DI Martino et al. (2022) ²³ Systematic review with 7 relevant articles	NR	NR	Before: 7.1 ± 1.2 After: 1.8 ± 2	VAS with unclear scale	NR	Reported by Akeda et al. (2011)
	NR	NR	Before: 66 ± 13.2 After: 43.3 ± 25.7	VAS with unclear scale	NR	Reported by Navani et al. (2016) and Levi et al. (2016)
	NR	NR	Before: 84 ± 11 After: 8 ± 17	VAS with unclear scale	NR	Reported by Kirchner et al. (2016)

Author (year) and study design	Results					
	Time points	Statistics	Effect size	Method of measurement	P	Notes
	NR	Mean with unclear variability measure	Before: 75 ± 13 After: 32 ± 24	VAS with unclear scale	NR	Reported by Akeda et al. (2017)
Xuan et al. (2020) ²⁴ Systematic review with 3 RCTs	Within 8 weeks	Pooled MD (95% CI)	-1.47 (-2.12 to -0.81)	NR	< 0.0001	Intervention-control, from meta-analysis with 2 studies
Sanapati (2018) ²⁵ Systematic review with 15 relevant articles	6 months	Pooled MD (95% CI)	-40.63 (-68.07 to -13.19)	VAS or NRS ranges from 0 to 100	0.004	Before-after the lumbar disc PRPI, from meta-analysis with 5 studies
	12 months	Pooled MD (95% CI)	-36.41 (-52.31 to -20.51)	VAS or NRS ranges from 0 to 100	< 0.001	Before-after the lumbar disc PRPI, from meta-analysis with 3 studies
	6 months	Pooled MD (95% CI)	-60.28 (-79.27 to -41.29)	Unclear tool ranges from 0 to 100	< 0.001	Before-after the epidural PRPI, from meta-analysis with 3 studies
Over 50% pain relief (pain score decreased > 50% from baseline)						
Peng et al. (2023) ²² Systematic review with 6 articles: 3 RCTs and 3 perspective cohort studies	1 month	Incidence rates (95% CI)	51.0% (0.17 to 0.84)	NA	NR	Before-after, transferred from OR
	2 months	Incidence rates (95% CI)	53.1% (0.21 to 0.83)	NA	NR	Before-after, transferred from OR
	6 months	Incidence rates (95% CI)	51.9% (0.41 to 0.63)	NA	NR	Before-after, transferred from OR
Xuan et al. (2020) ²⁴ Systematic review with 3 RCTs (2 included in	3 months	Pooled risk ratio (95% CI)	4.14 (2.22 to 7.74)	NA	< 0.001	Intervention-control, from meta-analysis with 2 studies

Author (year) and study design	Results					
	Time points	Statistics	Effect size	Method of measurement	P	Notes
the meta-analysis)						
Over 30% pain relief (pain score decreased > 30% from baseline)						
Peng et al. (2023) ²² Systematic review with 6 articles: 3 RCTs and 3 perspective cohort studies	1 month	Incidence rates (95% CI)	57.3% (0.32 to 0.80)	NA	NR	Before-after, transferred from pooled OR
	2 months	Incidence rates (95% CI)	50.7% (0.19 to 0.82)	NA	NR	Before-after, transferred from pooled OR
	6 months	Incidence rates (95% CI)	65.6% (0.48 to 0.80)	NA	NR	Before-after, transferred from OR

CI = confidence interval; NA = not applicable; NR = not reported; VAS = Visual analogue scale; NRS = Numerical Rating Scale; RCTs = randomized controlled trials; PRP = platelet-rich plasma; LBP = lower back pain; MD = mean difference; SMD = standardized mean difference.

Table 5: Summary of Findings by Outcome – Disability

Author (year) and study design	Results					
	Time points	Statistics	Effect size	Method of measurement	P	Notes
Disability score Changes						
*DI Martino et al. (2022) ²³ Systematic review with 7 relevant articles	Baseline; 3 months; 6 months	NR	Baseline: 27.9 ± 8.5 3 months: 10.5 6 months: 8.5 ± 8.81	ODI with unclear scale	NR	Reported by Kumar et al. (2015); PRP epidural injections
	Baseline; 3 months; 6 months	NR	Baseline: 22.0 ± 8.3 3 months: 11.2 ± 10.2 6 months: 11.7 ± 9.2	ODI with unclear scale	NR	Reported by Becker et al. (2007); PRP epidural injections
	Baseline; 3 months	NR	Baseline: 49.2 ± 9.624 3 months: 29.5 ± 11.65	ODI with unclear scale	NR	Reported by Bhatia and Chopra (2016); PRP epidural injections
Disability score decreased by 30% from the baseline						
Peng et al. (2023) ²² Systematic	2 months	Incidence rates (95% CI)	40.2% (0.26 to 0.56)	ODI with unclear scale	NR	Before-after, transferred from pooled OR

Author (year) and study design	Results					
	Time points	Statistics	Effect size	Method of measurement	P	Notes
review with 6 articles: 3 RCTs and 3 perspective cohort studies						
Disability score decreased by 50% from the baseline						
Peng et al. (2023) ²² Systematic review with 6 articles: 3 RCTs and 3 perspective cohort studies	6 months	Incidence rates (95% CI)	53.9% (0.42 to 0.67)	ODI with unclear scale	NR	Before-after, transferred from pooled OR

CI = confidence interval; NR = not reported; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire.

^aData from appendix table 11 in the included systematic review.²³

Table 6: Summary of Findings by Outcome – Patient Satisfaction

Author (year) and study design	Results					
	Time points	Statistics	Effect size	Method of measurement	P	Notes
Xuan et al. (2020) ²⁴ Systematic review with 3 RCTs (2 included in the meta-analysis)	NR	Pooled RR (95% CI)	1.91 (1.04 to 3.53)	NA	0.04	Intervention vs. control “offers relatively good patient satisfaction.” (page 531)

CI = confidence interval; NA = not applicable; NR = not reported; RR = risk ratio.

Table 7: Summary of Findings by Outcome – Adverse Events

Author (year) and study design	Results					
	Time points	Statistics	Effect size	Method of measurement	P	Notes
Xuan et al. (2020) ²⁴ Systematic review with 3 RCTs (2 included in the meta-analysis)	NR	Pooled RR (95% CI)	1.92 (0.94 to 3.91)	NA	0.07	Intervention vs. control

CI = confidence interval; NA = not applicable; NR = not reported; RR = risk ratio.

Appendix 5: Overlap Between Included Systematic Reviews

Note that this appendix has not been copy-edited.

Table 8: Overlap in Relevant Primary Studies Between Included Systematic Reviews

Primary study citation	Peng (2023) ²²	Di Martino (2022) ²³	Xuan (2020) ²⁴	Sanapati (2018) ²⁵
Goyal T, Paswan AK, et al. J Musculoskelet Res. 2022; 25:2250009.	Yes	–	–	–
Zielinski MA, Evans NE, et al. Pain Physician. 2022; 25:29 to 34.	Yes	–	–	–
Jain D, Goyal T, et al. Pain Med. 2020; 21:2719 to 25.	Yes	–	–	–
Navani A, Ambach MA, et al. IPM Reports. 2018; 2:111 to 118.	–	–	–	Yes
Akeda K, Ohishi K, et al. Asian Spine J. 2017; 11(3):380 to 9.	Yes	Yes	–	Yes
Centeno C, Markle J, et al. J Exp Orthop. 2017; 4:38	–	–	–	Yes
Ko GD, Mindra S, et al. J Back Musculoskelet Rehabil. 2017; 30:363 to 370.	–	–	–	Yes
Singla V, Batra YK, et al. Pain Pract. 2017; 17(06):782 to 791.	–	–	Yes	Yes
Wu J, Zhou J, et al. Pain Pract. 2017; 17(07):914 to 924.	–	–	Yes	Yes
Bhatia R, Chopra G, et al. J Clin Diagn Res. 2016; 10:UC05-UC07.	–	–	–	Yes
Kirchner F and Anitua E. J Craniovertebr Junction Spine 2016; 7:250 to 256.	–	Yes	–	Yes
Levi D, Horn S, et al. Pain Med. 2016; 17(6):1010 to 22.	Yes	Yes	–	Yes
Monfett M, Harrison J, et al. Int Orthop. 2016; 40:1321 to 1328.	–	–	–	Yes
Tuakli-Wosornu YA, Terry A, et al. PM R. 2016; 8(01): 1 to 10.	Yes	Yes	Yes	Yes
Wu J, Du Z, et al. Pain Phys. 2016; 8;19(8;11):617 to 625	–	–	–	Yes
Kumar R, Goni VG, et al. Asian Spine J. 2015; 9:916 to 922.	–	–	–	Yes
Navani A and Gupta D. Tech Region Anesth Pain Management. 2015; 19:54 to 59	–	–	–	Yes
Navani A and Hames A. Tech Region Anesth Pain Management. 2015; 19(1 to 2):38 to 44.	–	Yes	–	–
Bodor M, Toy A, et al. Lecture Notes in Bioengineering. 2014; Berlin: Springer, no page information.	–	Yes	–	–
Akeda K, Imanishi T, et al. Spine J Meet Abstr. 2011; No page information.	–	Yes	–	–
Becker C, Heidersdorf S, et al. Spine (Phila Pa 1976). 2007; 32:1803 to 1808.	–	–	–	Yes

“–” = Not included.

Appendix 6: References of Potential Interest

Systematic Reviews – all relevant primary studies were captured in at least one other more comprehensive systematic review

- Schneider BJ, Hunt C, Conger A, et al. The effectiveness of intradiscal biologic treatments for discogenic low back pain: a systematic review. *Spine J.* 2022;22(2):226-237. [PubMed](#)
- Ambrosio L, Vadala G, Russo F, et al. Interventional Minimally Invasive Treatments for Chronic Low Back Pain Caused by Lumbar Facet Joint Syndrome: A Systematic Review. *Global Spine J.* 2023 May;13(4):1163-1179. [PubMed](#)
- Daste C, Laclau S, Boisson M, et al. Intervertebral disc therapies for non-specific chronic low back pain: a systematic review and meta-analysis. *Ther Adv Musculoskelet Dis.* 2021;13:1759720X211028001.
- Chang MC, Park D. The Effect of Intradiscal Platelet-Rich Plasma Injection for Management of Discogenic Lower Back Pain: A Meta-Analysis. *J Pain Res.* 2021;14:505-512. [PubMed](#)

Randomized Controlled Trials

- Singh G, Talawar P, Kumar A, Sharma R, Purohit G, Bhandari B. Effect of autologous platelet-rich plasma (PRP) on low back pain in patients with prolapsed intervertebral disc: A randomised controlled trial. *Indian J Anaesth.* 2023;67(3):277-282. [PubMed](#)
- Zhang J, Liu D, Gong Q, Chen J, Wan L. Intradiscal Autologous Platelet-Rich Plasma Injection for Discogenic Low Back Pain: A Clinical Trial. *Biomed Res Int.* 2022;2022:9563693. [PubMed](#)
- Won SJ, Kim DY, Kim JM. Effect of platelet-rich plasma injections for chronic nonspecific low back pain: A randomized controlled study. *Medicine (Baltimore).* 2022;101(8):e28935. [PubMed](#)
- Schepers MO, Groot D, Kleinjan EM, Pol MM, Mylenbusch H, Klopper-Kes AHJ. Effectiveness of intradiscal platelet rich plasma for discogenic low back pain without Modic changes: A randomized controlled trial. *Interventional Pain Medicine.* 2022;1(1):100011.
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- Abo Elfadl GM, Elawamy AM, Abedalmohsen AM, El Sayed AAE, Bahloul M, Ismail EA. Prophylactic use of platelet-rich plasma for post-spinal low back pain following gynecological surgery: a randomized clinical trial. *Braz J Anesthesiol.* 2021;05:05.
- Jain D, Goyal T, Verma N, Paswan AK, Dubey RK. Intradiscal Platelet-Rich Plasma Injection for Discogenic Low Back Pain and Correlation with Platelet Concentration: A Prospective Clinical Trial. *Pain Med.* 2020;21(11):2719-2725. [PubMed](#)

Non-Randomized Studies

- Singh C, Yadav S, Loha S, Prakash S, Paswan AK. Comparison of intra-articular lumbar facet joint injection of platelet-rich plasma and steroid in the treatment of chronic low back pain: A prospective study. *Journal of Orthopaedics, Trauma and Rehabilitation.* 2023.
- Machado ES, Ambach MA, Caldas JM, Wei JJ, Bredemeier M. Personalized multitarget biologic injection in the spine: prospective case series of multitarget platelet-rich plasma for low back pain. *Regen Med.* 2022;17(1):11-22. [PubMed](#)
- Akeda K, Takegami N, Yamada J, et al. Platelet-Rich Plasma-Releasate (PRPr) for the Treatment of Discogenic Low Back Pain Patients: Long-Term Follow-Up Survey. *Medicina (Kaunas).* 2022;58(3):16. [PubMed](#)

Additional References

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- Patel A, Koushik S, Schwartz R, et al. Platelet-Rich Plasma in the Treatment of Facet Mediated Low Back Pain: A Comprehensive Review. *Orthop Rev (Pavia).* 2022;14(4):37076. [PubMed](#)
 Note: excluded as not a systematic review as defined for Rapid response.

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