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# Platelet-Rich Plasma Injections for Chronic Tendinopathies in the Lower Extremities

Rapid Review

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## Abbreviations

| | |
|---|---|
| **MA** | meta-analysis |
| **PRP** | platelet-rich plasma |
| **PRPi** | platelet-rich plasma injection |
| **PT** | physiotherapy |
| **RCT** | randomized controlled trial |
| **SR** | systematic review |

## Key Messages

- Findings from systematic reviews describing comparative clinical evidence for platelet-rich plasma injections (PRPis) in the treatment of chronic tendinopathies of the lower extremities were mixed.
- The systematic reviews we identified were often unclear concerning the components or treatment protocols used in the administration of PRPi, which may have contributed to the lack of a clear demonstration of effect.
- The variety of patient populations, comparisons, and outcomes in the included systematic reviews may also have contributed to the mixed findings.
- The lack of a clear demonstration of the comparative clinical effectiveness of PRPi in chronic tendinopathies of the lower extremities does not currently support decision-making in favour of its use.

## Research Question

What is the clinical effectiveness of platelet-rich plasma injections (PRPis) for the treatment of adults with chronic tendinopathies in the lower extremities?

## Context and Policy Issues

### What Are Chronic Tendinopathies in the Lower Extremities?

Chronic, or persistent, tendinopathy is a common disorder that is characterized by pain and loss of function,[1] and has been described as accounting for 30% of musculoskeletal conditions.[2] Chronic tendinopathies represent a range of conditions, based on the location of the affected tendon, with chronic tendinopathies of the lower extremities occurring in the hip (e.g., gluteus), knee (e.g., patella), Achilles, and/or plantar fascia.[3-5] Chronic tendinopathies of the lower extremities can cause pain, swelling, and can interfere with the activities of daily life (including performance in exercise and sport), as well as quality of life.[2]

Causes of chronic tendinopathies may vary, but they are often believed to be the result of overuse[1,6] and/or impaired healing of an injury.[2,7,8] Risk factors for developing chronic tendinopathy include intrinsic factors, such as age and previous injury, and extrinsic factors, such as exposure to high-intensity exercise.[1]

### What Are PRPis?

Platelet-rich plasma (PRP) is a biologic treatment derived from blood products, and containing concentrated growth factors, which are thought to reduce inflammation and promote healing.[2,9] PRP has been described as a general term for therapy lacking standardization in its composition and administration.[10]

Multiple treatments are available for chronic tendinopathies — including those of the lower extremities — with conservative therapies including physiotherapy and/or systemic pharmacotherapy for pain.[3,11,12] Other nonsurgical treatments include injection therapies that may be used following more conservative therapies,

such as local anesthetic, corticosteroid, dry needling, or PRPis.[6,13] While PRPi are not thought to be curative, it has been hypothesized that pain and function may be improved in response to their administration.[13] PRPi has also been described as 1 of the most widely studied biologic therapies and can be used in surgical or nonsurgical settings.[14] Nonetheless, PRPi has also been described as a costly intervention, incurring greater expense versus comparable therapies,[15] and is not always reimbursed by payers or insurers.[16]

### Why Is It Important to Do This Review?

The incidence of chronic tendinopathies, in general, has been on the rise and is thought to be associated with greater participation in recreational exercise and sports among middle-aged individuals.[1] While no Canadian data on the incidence or prevalence of chronic tendinopathies in the lower extremities were identified, a survey of Canadian adults indicated the knee and leg as the third and fourth most common sites of chronic pain.[17] Notably, it has been suggested that tendinopathies of the lower extremities may respond differently to treatment than those of the upper extremities, based on factors associated with the central nervous system.[3]

Current recommendations for the nonsurgical management of chronic tendinopathies include physiotherapy and nonsteroidal anti-inflammatory drugs. Other treatment options, including PRPi, have been described as alternative treatments with limited evidence demonstrating clinical efficacy,[3,10] and making decisions concerning the use of PRPi in chronic tendinopathies of the lower extremities challenging.

In 2019, Health Canada clarified its classification of PRP as a drug, confirming its distinction from cell therapies.[18] Nonetheless, concern has been raised about this classification, which renders PRP broadly available in Canada despite the purported lack of evidence demonstrating its effectiveness.[19]

### Objective

To support decision-making about the use of PRPi in chronic tendinopathies of the lower extremities, we conducted this review to summarize recent, available evidence describing its clinical effectiveness.

## 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, as well as a focused internet search. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevancy. The search strategy comprised both 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 PRPis and tendinopathies. Conference abstracts were excluded. Retrieval was limited to the human population. The search was completed on May 8, 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.

### Table 1: Selection Criteria

| Criteria | Description |
|---|---|
| **Population** | Adults with chronic tendinopathies in the lower extremities (e.g., patellar tendinitis, peroneal tendinitis) |
| **Intervention** | Platelet-rich plasma injections |
| **Comparator** | Usual care (e.g., no treatment with platelet-rich plasma injections, exercise or physiotherapy, cortisone injections, nonsteroidal 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, were duplicate publications, or were published before 2018. Reports of acute tears and other injuries in which the tendon did not remain intact were interpreted as distinct from chronic tendinopathies and were therefore excluded.[1] Studies reporting PRPi comparisons with "alternative interventions" (i.e., not considered usual care), local anesthetic injections, whole blood injections, radiation, stem cell therapy, extracorporeal shockwave therapy and hyaluronic acid injection, as well as studies reporting no comparator (i.e., single-arm studies), were excluded. SRs in which all relevant studies were captured in other more recent or more comprehensive SRs were also excluded.

### Critical Appraisal of Individual Studies

The included publications were critically assessed by 1 reviewer using the A MeaSurement Tool to Assess systematic Reviews 2 (AMSTAR 2)[20] for SRs, with additional considerations applied to overviews of reviews. 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 408 citations were identified in the literature search. Following screening of titles and abstracts, 341 citations were excluded and 67 potentially relevant reports from the electronic search were retrieved for full-text review. There were no potentially relevant publications retrieved from the grey literature search for full-text review. Of these potentially relevant articles, 58 publications were excluded for various reasons,

and 9 publications met the inclusion criteria and were included in this report. These comprised 1 overview of systematic reviews[21] and 8 SRs.[22-29] Appendix 1 presents the PRISMA[30] flow chart of the study selection.

Additional references of potential interest are provided in Appendix 6.

## Summary of Study Characteristics

This review identified and summarized 1 overview of SRs[21] and 8 SRs.[22-29] Characteristics of included reviews are tabulated and detailed in Appendix 2.

Eight of the 9 reviews were broader in scope than the eligibility criteria for the current review[21-23,25-29] and so, only the subset of 37 unique included studies that were relevant to this report were summarized. Of the relevant included primary studies in the SRs, there was considerable overlap, which is characterized in a matrix presented in Appendix 5. In cases of overlap, the most comprehensive and/or recently published SRs were selected to inform the summary of relevant primary studies.

The included overview of SRs was conducted in the US and published in 2020, with a search that spanned database inception to February 2020.[21] The 8 included SRs were conducted in India,[23,25] Italy,[22,29] China,[24,27] UK,[26] and Poland,[28] and were published between 2018 and 2023 with search time frames that ranged from 1966 (or database inception) to December 2022, when reported.[22-29]

Patient populations included those with chronic tendinopathies of the hip,[23,26] patella,[25,28] Achilles,[21,23,24] and plantar fascia,[22,27,29] with ages either not reported[21,24,28] or with mean age ranging between 19 years and 62 years.[22,23,25-27,29] All of the reviews reported on comparative investigations of PRPi versus a variety of comparators, including saline or placebo injections,[21,24,25,28,29] steroids (either administered by injection or with mode of administration NR),[22,26,27,29] dry needling,[23,25,29] and/or physiotherapy (PT).[25]

Outcomes included measures of function, including the Victorian Institute of Sports Assessment (VISA) with versions specific to the Achilles (VISA-A) or patella (VISA-P),[21,25] Foot Function Index (FFI),[22,28,29] or the American Orthopedic Foot and Ankle Society (AOFAS) score.[29] Pain was reported by the 8 SRs, all of which described the use of the visual analogue scale (VAS) for measurement.[22-29] Three SRs described composite measures (combining function, pain, and other measures), including the VISA-Achilles (VISA-A),[24] Harris Hip Score (HHS),[26] and AOFAS score.[27] Other outcomes included a return to exercise and/or sport,[24] patient satisfaction,[24] quality of life (QoL),[25] and adverse events.[25,27] Two SRs did not specify all outcomes that were measured; rather only provided the names of the measures that were used,[23,29] including the VISA[23,29] and the Foot and Ankle Ability Measurement (FAAM);[29] for these unspecified outcomes, the VISA was interpreted as a composite measure and the FAAM was interpreted as a measure of function in this report. One SR did not report on all of the measure(s) that were used, describing only the outcome; that is, pain.[23] Follow-up of outcomes ranged from between 1 week to 24 months in the 8 included SRs,[22-29] but was not reported in the overview of SRs.[21]

## Summary of Critical Appraisal

### Reporting

All of the included reviews provided some description of their inclusion criteria;[21-29] however, 3 reviews did not describe either the establishment of an a priori method or development of a review protocol.[21,26,29] A preestablished method is important for informing the conduct of reviews and allows readers to assess any protocol deviations that could introduce a risk of bias to the findings of the review.[20] The rationale for limiting inclusion of study designs was either not reported or not explicitly stated by the 8 included SRs,[22-29] whereas the overview of SRs did describe an implicit rationale for limiting included studies to SRs.[21]

Included studies were described in sufficient detail by 1 SR,[25] while some information describing the intervention and/or comparator(s) (e.g., number of injections, dose, frequency) was missing in 7 reviews.[21-24,26-28] Two reviews had information missing on either the outcomes measured (i.e., including only the outcome measure without a description of what was being measured) or the measures used.[23,29] One SR described patient satisfaction but did not provide detail as to how this outcome was measured, or what precisely was being measured.[24]

Three of the included SRs reported their funding sources,[24,27,28] and 4 reported that no funding was received to support the conduct of the review.[21,23,25,26] Two reviews did not report any information about source(s) of funding.[22,29] This information is important for assessing any potential conflict of interest or risk of bias introduced by funding source(s).

Finally, the overview of SRs reported an analysis of overlap between primary studies in its included SRs.[21]

### Search Strategy

While all of the included reviews performed searches in 2 or more relevant databases,[21-29] and all but 1[21] reported the search keywords used,[22-29] only 1 SR described consultation with an expert biomedical librarian in the development of the search strategy.[23] A comprehensive search should draw from the expertise of an information specialist or scientist to ensure that the strategy uses adequate search terms and is sufficiently sensitive and specific.[20] And while search time frames were clearly and explicitly reported by 4 of the included reviews,[21,23,24,27] 5 SRs did not clearly or completely report the dates of the search(es) conducted.[22,25,26,28,29]

### Review Methods

Study selection was performed by 2 independent reviewers in 7 included reviews,[21,23-27,29] whereas 2 reported no information on the number of reviewers that performed study selection.[22,28] Five reviews reported that data abstraction was performed by 2 independent reviewers,[21,22,25,26,29] and 4 of them either reported no information on the number of reviewers who completed data abstraction, or reported that it was performed by 1 reviewer.[23,24,27,28] Similarly, while risk of bias (RoB) assessments were reported by all of the 9 included reviews summarized in this report,[21-29] and 2 independent reviewers performed the assessments in 8 included reviews,[21-23,25-29] 1 SR did not describe whether the assessments were performed in duplicate or not.[24] Duplicate study selection, data abstraction and RoB assessment are important features of a robust method that reduce the risks of error and bias in the review.[20]

Appropriate statistical methods were described for carrying out meta-analyses by 6 of the 7 SRs that performed them,[22,24-27,29] whereas 1 did not describe methods in detail.[28] For the 7 reviews that performed quantitative syntheses, 2 described assessment of the risk of publication bias,[22,24] though, none provided a description of the potential impact of publication bias on the findings of the reviews.[22,24-29]

Heterogeneity between the included studies and its potential impact on the findings of the review was reported in sufficient detail by 3 of the included reviews,[26,27,29] while 6 made a cursory mention of heterogeneity and/or did not describe its potential impact on the review findings.[21-25,28]

Additional details regarding the strengths and limitations of included reviews are provided in Appendix 3.

## Summary of Findings

### Clinical Effectiveness of PRPIs

#### *Function*

Measures of function were reported by 5 reviews, with 1 describing tendinopathy of the Achilles,[21] 2 describing knee tendinopathies[25,28] and 2 describing plantar fasciitis.[22,29] Generally, findings describing function were mixed, with most findings describing no difference between PRPi and comparators, some indicating that PRPi was superior to comparators, and 1 reporting that saline injections were superior to PRPi.[21,22,25,28,29]

The overview of SRs reported on function of the Achilles tendon, and found no difference between PRPi and saline groups at an unspecified duration of follow-up (1 SR with 4 randomized controlled trials [RCTs], 170 patients; Table 6).[21]

Of the 2 SRs reporting on function of the knee, 3 relevant RCTs were described (Table 6):

- There were no statistically significant differences in VISA-P scores between PRPi and dry needling at short-term (8 to 12 weeks) or 6 month follow-up (1 RCT with 19 patients).[25]
- PRPi compared to saline injections showed mixed results.[25,28]
  - One RCT found no statistically significant difference in VISA-P scores of 38 patients at short-term (8 to 12 weeks) or 6 months follow-up, but reported a statistically significant improvement in the control group at 1 year of follow-up.[25]
  - One RCT included 36 patients and found a statistically significant improvement in VISA scores in the PRPi group at 6 months of follow-up.[28]

Of the 2 SRs reporting on function in plantar fasciitis (based on 5 RCTs), neither provided supporting data, and mixed conclusions were observed (Table 6):

- PRPi was described as more effective than saline or dry needling for improving function (2 RCTs with 150 patients).[29]
- PRPi was described as either no different than steroids (1 RCT with 79 patients[22] and 1 RCT with 30 patients[29]), or more effective than steroids for improving function (1 RCT with 80 patients).[29]

### *Pain*

Eight SRs reported on pain.[22-29] Two of the 8 included SRs described pain in chronic tendinopathies of the hip,[23,26] 2 in the knee,[25,28] 2 in the Achilles tendon,[23,24] and 3 in plantar fasciitis.[22,27,29] Overall, findings describing pain were mixed, with most describing no difference between PRPi and control groups, some indicating that PRPi was superior to comparators, and 1 reporting that dry needling was superior to PRPi.[22-29]

Of the 2 SRs describing chronic tendinopathy of the hip, findings from 1 RCT[23] and a meta-analysis (MA) of 2 RCTs[26] were reported (Table 7):

- One RCT compared PRPi to dry needling in 30 patients, reporting both interventions as "equally effective" at reducing pain at up to 2 weeks of follow-up (i.e., specific timing was not specified).[23]
- An MA of 2 RCTs comparing PRPi to steroids in 124 hips found no statistically significant difference in pain scores between groups at 2 to 6 months of follow-up.[26]

Of the 2 SRs describing pain in chronic tendinopathy of the knee, findings from 2 RCTs and 1 nonrandomized study (NRS),[25,28] were reported (Table 7):

- One RCT compared PRPi to dry needling in 19 patients, reporting a statistically significant improvement in pain scores in the control group at 6 months of follow-up.[25]
- One NRS compared PRPi to PT in 31 patients, reporting no statistically significant differences between groups at short-term (i.e., 8 to 12 weeks) or 6 months of follow-up.[25]
- Another RCT compared PRPi to saline in 36 patients, reporting a statistically significant improvement in pain scores for those who received PRPi at 6 months of follow-up.[28]

Of the 2 SRs describing pain in chronic tendinopathies of the Achilles, findings from 1 RCT[23] and 4 MAs of 3 RCTs[24] were reported (Table 7):

- One RCT of 84 patients comparing PRPi and dry needling showed that VAS scores were numerically similar between groups; however, study authors concluded that PRPi was slightly superior to dry needling for reducing pain, particularly in younger patients.[23]
- The MAs of 3 RCTs comparing PRPi to placebo in 93 patients found:
  - no statistically significant differences between groups in pain scores at 6 weeks or 6 months of follow-up
  - a statistically significant improvement in pain scores for patients who received PRPi at 3 months of follow-up, as well as in a combined MA of data across all 3 follow-up time points (reported as 279 patients).[24]

Of the 3 SRs describing pain in plantar fasciitis, findings from 4 RCTs,[22,29] and 2 MAs,[27,29]were reported (Table 7):

- One RCT and both MAs reported no differences in pain between PRPi and steroids,[22,27] whereas another RCT found an improvement in patients who received PRPi as compared to steroids[29]
- One SR concluded (without providing supporting data) that there was an improvement in patients who received PRPi as compared to the following:

- dry needling in 30 patients at 3 months of follow-up (1 RCT)
- saline in 120 patients at 6 months of follow-up (1 RCT).[29]

### *Composite Measures*

Composite measures were reported by 5 SRs with 1 describing chronic tendinopathy of the hip,[26] 2 the Achilles tendon,[23,24] and 2 plantar fasciitis[27,29] (Table 8). Overall, findings were mixed, with several demonstrating no effect of PRPi, some indicating a clinical improvement in patients who received PRPi and 1 reporting a comparative improvement in patients receiving steroids.

- There was a statistically significant improvement in a composite measure of function, pain and range of motion in hips that received PRPi as compared to steroids at a follow-up of 2 to 6 months (MA of 3 primary studies; 124 hips).[26]
- Whereas 1 RCT in 1 SR reported a "marginal improvement" in VISA-A scores in patients with Achilles tendinopathy who received PRPi as compared to dry needling (no statistical testing reported),[24] another SR indicated there were no statistically significant differences between PRPi or placebo in VISA-A scores (4 MAs of 6 to 8 RCTs).[23]
- The SRs describing a comparison of PRPi with steroids[27,29] in plantar fasciitis, reported the following:
  - no statistically significant difference was observed between groups in AOFAS scores (MA of 5 RCTs; 356 patients)[27]
  - a statistically significant improvement in the AOFAS scores of the control group (MA of 3 RCTs; 252 patients)[27] and that PRPi was "more effective," as measured by VISA scores, than steroids (1 RCT; 80 patients) (data not provided).[29]

### *Return to Exercise and/or Sport*

For patients with chronic tendinopathy of the Achilles, there were no statistically significant differences in return to exercise and/or sport between PRPi and placebo at 2 to 46 weeks of follow-up (1 SR with MA of 4 RCTs; Table 9).[24]

### *Patient Satisfaction*

For patients with chronic tendinopathy of the Achilles, there were no statistically significant differences in patient satisfaction between PRPI and placebo at 2 to 48 weeks of follow-up (1 SR with MA of 4 RCTs, 222 patients; Table 10).[24]

### *Quality of Life*

For patients with chronic tendinopathy of the knee, there were no statistically significant differences in QoL between PRPi and the control group at 8 to 12 weeks or 6 months of follow-up (1 SR with MA of 1 RCT and 1 NRS; Table 11).[25] Of note, the 2 primary studies included in the MAs used different QoL measures (EQ-VAS and SF-12) and different comparators (i.e., dry needling and PT).[25]

### *Adverse Events*

Of the 2 SRs reporting on adverse events,[25,27] findings from 3 primary studies in 1 SR[25] and 5 RCTs in the other[27] indicated that no adverse events were observed in either the PRPi or comparator groups[25,27] (Table 12).

## Limitations

The literature describing PRPi treatment in chronic tendinopathies of the lower extremities is ample, with a broad variety of conditions, treatment protocols, comparators, and outcomes described. Two of the key limitations identified in this review of the literature on this topic included SRs describing primary studies with small sample sizes and variable findings, as well as a lack of clarity and standardization in the reporting and descriptions of interventions, comparators, outcomes, and measures.

The overview of SRs included in this report identified 1 unique SR of relevance to this report that summarized 4 RCTs describing 170 patients (with no detail on the sample sizes of each of the RCTs described).[21] The 8 SRs identified and summarized in this report included 36 unique primary studies of relevance,[22-29] with 7 of these SRs including primary studies with sample sizes ranging between 19 and 120 patients,[22-25,27-29] and 1 SR reporting a range of 20 to 80 hips (rather than patients as the unit of analysis).[26] The expanding number of primary research studies with small sample sizes and effect sizes has been identified as a challenge to decision-making about optimal approaches to its use in other papers, as well,[15] corroborating the findings of this review.

A lack of clarity in the description of chronic tendinopathies in the literature was observed, with broad references to tendinopathies, diseases or disorders often leaving it unclear as to whether the condition(s) being described were chronic or acute, for instance. This made the interpretation of some of the literature on this topic challenging and unclear as it concerned the populations of interest.

Variability in reporting was also a limitation identified in this review; for instance, authors of 1 included SR acknowledged that PRPi is described inconsistently in the literature, making interpretation of the composition of the intervention (e.g., leukocyte concentration) and treatment protocols challenging, and creating the potential to produce variable findings.[26] In this report, inconsistency was observed in the description of the use of PRPi, with several reviews not reporting on key features of the intervention, such as number(s) of injections, dose(s), frequency of injections, and/or intervals between multiple injections.[21-23,26-28] Similarly, comparator arms of relevant primary studies were not described sufficiently to understand their composition in most of the included reviews.[21,22,24,26-29] These deficits in reporting leave uncertainty as to whether any possible differences in PRPi or comparison treatment protocols may have contributed to the variability in the findings of SRs included in this review. For instance, if 1 PRPi injection was used in some of the study treatment protocols, whereas multiple injections were used in another, the findings of these studies may have been impacted; however, because insufficient information was provided, the potential for this variability to impact findings and interpretation cannot be ascertained.

Likewise, unclear reporting of the outcomes and/or measures used in the included reviews was a limitation observed in this review.[21-29] For instance, while 2 of the SRs included in this review reported the use of the VISA score, the outcome being measured was not described,[23,29] necessitating an assumption as to the outcome being measured. In addition, whereas 3 reviews described the use of the VISA as a measurement of function,[21,25,28] another described the VISA as a composite measure of pain function and activity.[24] This variability in the description of what was measured in the reviews summarized in this report limits the clarity and interpretation of its findings.

In addition, there was a lack of evidence describing a comparison of PRPi with nonsteroidal anti-inflammatory drugs (NSAIDs), and limited evidence describing a comparison of PRPi with PT. Given that these treatments have been described as first-line, conservative therapies in the usual care of chronic tendinopathies,[3] this lack of evidence describing their comparative clinical effectiveness with PRPi is a limitation of this report.

Finally, none of the 9 reviews summarized in this report were conducted in Canada.[21-29] Further, while 7 of the reviews did not describe the countries within which the primary studies were conducted,[21-23,26-29] 2 SRs described relevant primary studies from countries outside Canada only.[24,25] This apparent lack of Canadian data may limit the generalizability of the findings of this report to the Canadian context.

## Conclusions and Implications for Decision- or Policy-Making

This report identified and summarized 1 overview of SRs[21] and 8 SRs of primary studies[22-29] describing the clinical effectiveness of PRPi for chronic tendinopathies of the lower extremities.

Findings across the included reviews and their relevant included studies were variable, with many of the reported findings demonstrating no observed comparative effect(s) of PRPi in chronic tendinopathies of the lower extremities.[21-27,29] Nonetheless, 4 reviews described findings that did demonstrate clinical improvement in patients to whom PRPi were administered,[24,26,28,29] and 2 SRs reported findings that demonstrated clinical improvement in patients to whom control interventions were administered.[25,27] It is possible that this variability in findings and conclusions may have been impacted by the variability in patient populations (i.e., various tendinopathies), interventions (e.g., various treatment protocols) and comparators (e.g., placebo and/or various active treatments) — as well as a variety of outcomes and measures. Nonetheless, there was no clear pattern of clinical effectiveness that could be identified among subgroups of patient populations, comparisons, or outcomes.[21-29]

The proliferation of studies investigating the use of PRPi for chronic tendinopathies in recent years has been analyzed and commented on repeatedly in the literature;[14,15,31] similarly, the lack of consensus and certainty as to its clinical effectiveness has been highlighted.[8,32,33] Factors contributing to this uncertainty have been outlined in the relevant literature, and are similar to those identified in this report, for example, small RCTs of limited quality with no or small effect sizes,[2,6,8,34,35] as well as considerable lack of clarity and/or variability in PRPi components and treatment protocols,[6,8,9,14,35-38] which has been identified as a challenge to drawing conclusions from the research investigating its effectiveness. On the other hand, this report identified several

MAs that provide a more robust estimate of the clinical effectiveness of PRPi for chronic tendinopathies than is provided by smaller RCTs; though few demonstrated a statistically significant improvement in function among patients receiving PRPi.

CADTH has conducted past reviews of the clinical evidence describing PRPi for other indications, including orthopedic conditions, trauma[39] and low back pain.[40] While the conditions reviewed in those reports are not entirely relevant to the research question posed in this report, it is notable that both reports similarly identified a lack of conclusive evidence supporting the clinical effectiveness of PRPi, with both indicating some evidence to support its safety, but a lack of evidence to support efficacy.[39,40]

Despite the variability of the findings in the literature summarized in this review, there may be potential for clinical effectiveness of PRPi, given that some of the findings summarized herein have demonstrated effectiveness. Specifically, 1 MA of 3 primary studies assessing pain in the Achilles tendon demonstrated a statistically significant improvement in patients who received PRPi as compared to placebo;[24] and another MA of 3 primary studies investigating the comparative effectiveness of PRPi versus steroids in patients with chronic tendinopathy of the hip demonstrated a clinical improvement in patients who received PRPi.[26] It may be that advances in the technology of platelet-rich therapies, such as platelet-rich fibrin[41] and plasma gel[42] could hold promise for clearer or more consistent improvement in clinical outcomes among musculoskeletal conditions. Nonetheless, measurement of effectiveness that can support clinical and other decisions concerning the use of PRPi in chronic tendinopathies is necessarily supported by high-quality RCTs that use robust methods with sufficient sample sizes and standardized treatment protocols, which remain a current limitation of the literature on this topic.[9,43] The inconclusive state of the current evidence describing PRPi for chronic tendinopathies, combined with its high cost, has been highlighted as a point of caution in interpreting the evidence — including assertions that the available evidence does not support the current use of PRPis.[15,44]

Given the inconsistency across the findings reported in the current literature summarized in this report that describes the comparative clinical effectiveness of PRPis in chronic tendinopathies of the lower extremities, the evidence is likely insufficient at this time to support decision-making in favour of its use.

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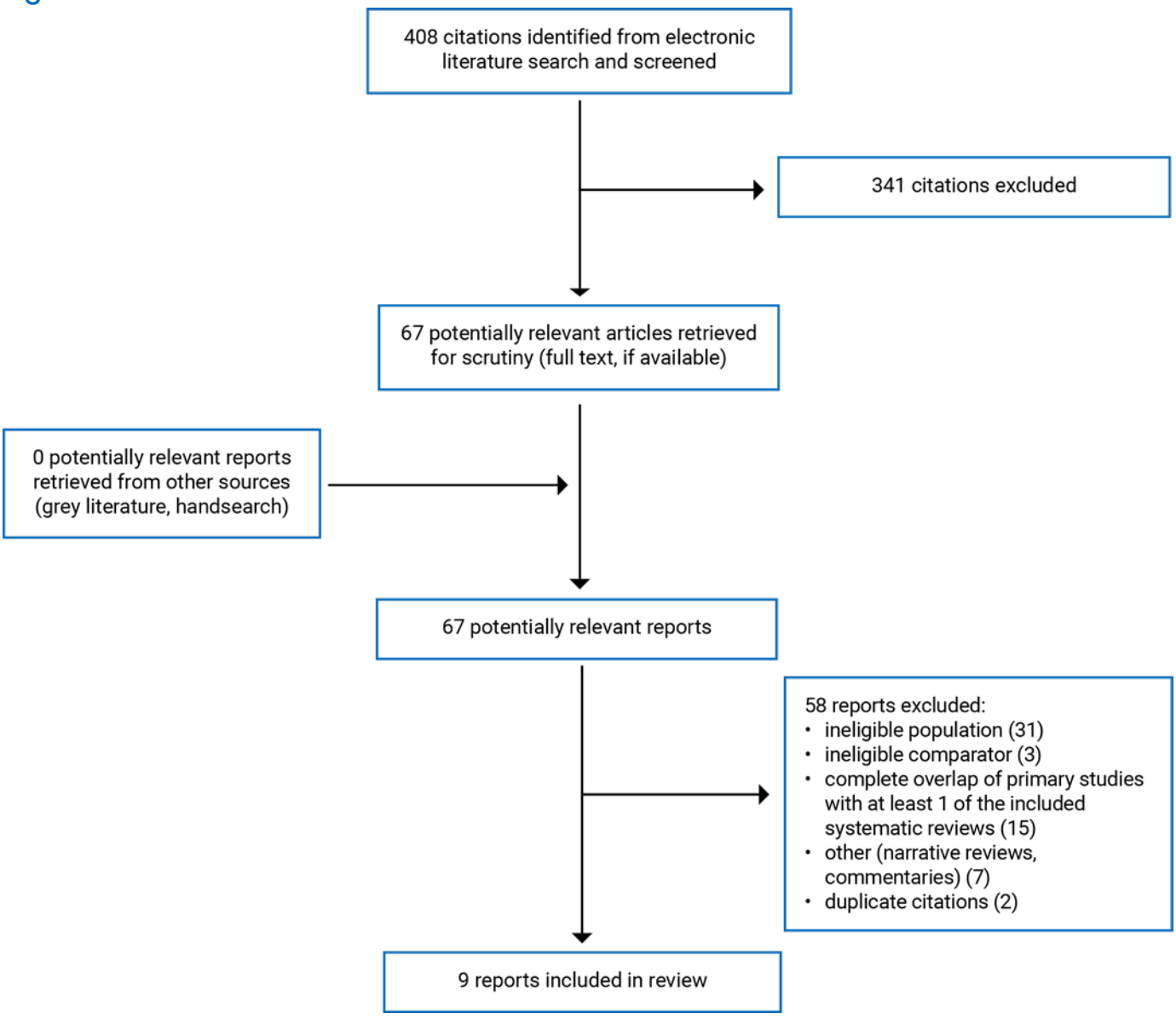
# Appendix 1: Selection of Included Studies

## 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 Overview of 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 |
|---|---|---|---|---|
| Irby et al. (2020)[21]<br>US<br>**Funding source:**<br>Reported as none | SRs eligible for and summarized in this report: 1 of 25 included SRs<br>Sources and dates searched:<br>The sources searched were PubMed, Embase, CINAHL, Physiotherapy Evidence Database (PEDro), and the Cochrane Database from database inception to February 2020 | Included studies: 4 RCTs<br>Patients: 170 patients with Achilles Tendinopathy<br>Intervention group = 85<br>No other characteristics reported<br>Comparator group = 85<br>No other characteristics reported | Intervention:<br>PRPi<br>N injection(s), dose, frequency, interval(s) between injections = NR<br>Comparator:<br>Saline injections<br>N injection(s), dose, frequency, interval(s) between injections = NR | Outcome (measure): Function (VISA-A)<br>Follow-up: NR |

CINAHL = Cumulated Index to Nursing and Allied Health Literature; PEDRo = Physiotherapy Evidence Database; NR = not reported; PRPi = platelet-rich plasma injection; RCT = randomized controlled trial; SR = systematic review; VISA-A = Victorian Institute of Sports Assessment–Achil

VISA-A: The VISA-A is scored using a numeric scale from 0 to 100, with 100 representing no symptoms and lower scores more deleterious symptoms.[45]

## Table 3: 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 |
|---|---|---|---|---|
| Masiello et al. (2023)[22]<br>Italy<br>**Funding source:**<br>NR | Primary studies eligible for this review: 9 of 33 included RCTs<br>Primary studies summarized in this report: 1 of the 9 eligible RCTs that were not included in the other SRs included in this report.<br>Sources and dates searched: The sources searched were MEDLINE, Embase, SCOPUS, OVID, and the Cochrane Library databases from an unspecified time point to November 2021 | All eligible patients, N = 79<br>Plantar fasciitis, n = 79<br>Age, range = 19 to 62 yr<br>Intervention group = 39<br>No other characteristics reported.<br>Comparator group = 40<br>No other characteristics reported | Intervention: PRPi<br>N injections, dose, frequency, interval(s) between injections = NR<br>Comparator: Steroid<br>Mode of administration, dose, frequency = NR | Outcomes (measure): Pain (VAS); function (FFI)<br>Follow-up: 36 months |
| Nuhmani et al. (2023)[23]<br>India<br>**Funding source:**<br>Reported as 'Nil' | Primary studies eligible for this review: 3 of 7 included RCTs<br>Primary studies summarized in this report: 2 of the 3 eligible RCTs that were not included in the other SRs included in this report.<br>Sources and dates searched: PubMed, Web of Science, Scopus, and SPORTDiscus databases from 1999 (month NR) to October 2020 | All eligible patients: N = 126<br>Patients with Achilles tendinopathy = 84 (1 RCT)<br>Intervention group = 46<br>Male = 26<br>Female = 20<br>Age, mean (SD) = 42.4 (14.6)<br>Comparator group = 38<br>Male = 20<br>Female = 18<br>Age, mean (SD) = 43 (12)<br>Greater trochanteric pain syndrome = 42 (1 RCT)<br>Intervention group = 30<br>Male = 6<br>Female = 24 | Intervention: PRPi<br>N injections, dose, frequency, interval(s) between injections = NR<br>Comparator: Dry needling<br>N injections = range 1 to 3<br>Interval between multiple injections = 1 wk | Outcomes (measures): Pain (NR; VAS), NR (VISA-A)<br>Follow-up: Baseline, postintervention (i.e., 1wk and 2wk; 3mo and 6 months) |

| 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 |
|---|---|---|---|---|
| | | Age, mean (SD) = 60 (13.06)<br>Comparator group = 12<br>Male = NR<br>Female = NR<br>Age, mean (SD) = 53 (12.6) | | |
| Vithran et al. (2023)[24]<br>China<br>**Funding sources:**<br>National Key R&D Program of China (No. 2019YFA0111900); National Natural Science Foundation of China (No. 81874030, 82072506); Hunan Young Talents of Science and Technology (No. 2021RC3025); Provincial Clinical Medical Technology Innovation Project of Hunan (No. 2020SK53709); Innovation-Driven Project of Central South University (No.2020CX045); Wu Jieping Medical Foundation (No. 320.6750.2020 to 03 to 14) | Primary studies eligible for and summarized in this report: All 8 included RCTs.<br>Sources and dates searched: The sources searched were PubMed, Embase, Cochrane Library, Web of Science, China Biomedical CD-ROM, and Chinese Science and Technology Journal databases from January 1966 to December 2022 | All patients: N = 491<br>Achilles tendinopathy = 491<br>Duration of condition, range = > 2mo to a mean of 33 months<br>Intervention groups = 244<br>No other characteristics reported.<br>Comparator groups = 247<br>No other characteristics reported | Intervention: PRPi<br>N injections, range = 1 (7 RCTs) to 4 (1 RCT)<br>Interval between multiple injections = 2 wk (1 RCT)<br>Dose, range = 3 to 5<br>Comparator: Placebo i.e., saline (5 RCTs); blank (3 RCTs)<br>N injections, frequency, dose = NR/NA | Outcomes (measure): Composite measure of pain, function and activity (VISA-A), pain (VAS), patient satisfaction (n patients satisfied), return to exercise (n/N patients)<br>Follow-up: 2 to 48 wk |
| Barman et al. (2022)[25]<br>India<br>**Funding source:**<br>Reported as none | Primary studies eligible for and summarized in this report: 3 (2 RCTs and 1 NRS) of 8 included RCTs and NRS<br>Sources and dates searched: The sources searched were PubMed, MEDLINE, Embase, CINAHL, and Cochrane Central Register of Controlled Trials | All patients, N = 111<br>Patellar tendinopathy = 111<br>Average age, range = 27.1 to 34 yr<br>Male-female ratios, range = 1:0 to 19:1<br>Intervention groups = 63<br>No other characteristics | Intervention: LR-PRPi, with (1 RCT, 1 NRS) or without (1 RCT) dry needling (1 RCT) or PT (1 NRS)<br>N injections, range = 1 (2 RCTs) to 3 (1 NRS)<br>Interval between multiple injections = 15 d<br>Dose, range = 3.5 to 6 mL | Outcomes (measures): Function (VISA-P); pain (VAS); QoL (SF-12; EQ-VAS); safety (adverse events)<br>Follow-up: Minimum mo, range = 6 to 12 |

| 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 |
|---|---|---|---|---|
| | databases from an unspecified time point to November 2021 | reported.<br>Comparator groups = 45<br>No other characteristics reported | Comparator: Saline (1 RCT); dry needling (1 RCT); PT (1 NRS)<br>Saline, N injections, dose = 1, 3.5 mL<br>Dry needling, N episodes, = 1<br>PT, N episodes = NR | |
| Migliorini et al. (2021)[26]<br>UK<br>**Funding source:**<br>Reported as none | Primary studies eligible for and summarized in this report: 4 of 7 included RCTs.<br>Sources and dates searched: The sources searched were PubMed, Embase, Google Scholar and Scopus databases with no search time frame specified (authors report only that the search was conducted in December 2020) | All hips, N = 172<br>Greater trochanteric pain syndrome = 172<br>Intervention groups = 86<br>% female, range = 30 to 91.7<br>Mean age, range = 48.7 to 60.3<br>Comparator groups = 86<br>% female, range = 66.6 to 95.0<br>Mean age, range = 48.7 to 56.3 | Intervention: PRPi<br>N injections = NI[a] (4 RCTs)<br>Interval between multiple injections, dose = NR (4 RCTs)<br>Comparator: Steroid injection (3 RCTs); saline (1 RCT)<br>Steroids, type, N injections, dose = methylprednisolone, 1, NR (1 RCT); triamcinolone, 1, NR (1 RCT); NR, Ni[a], NR (1 RCT)<br>Saline, N injections, dose = 1, 3.5 mL (1 RCT) | Outcomes (measure): Composite of function, pain, RoM (HHS); pain (VAS)<br>Follow-up: 2 to 12 months |
| Huang et al. (2020)[27]<br>China<br>**Funding sources:**<br>National Natural Science Foundation of China (grant 81871792); Scientific and Technological Plan of Traditional Chinese Medicine of Zhejiang Province (grant 2018ZB033); Medical and Health Science and Technology Project of Zhejiang Province (grants 2018KY324, 2020KY498) | Primary studies eligible for and summarized in this report: 12 of 20 included RCTs.<br>Sources and dates searched: The sources searched were Cochrane Bone, Joint and Muscle Trauma Group Specialized Register, the Cochrane Central Register of Controlled Trials, MEDLINE, Embase, Web of Science, and the Cochrane Library from database inception to October 2018 | All eligible patients, N = 613<br>Plantar fasciitis = 613<br>Male[b] = 181<br>Female[b] = 331<br>Mean age, range = 31 to 59 yr<br>Symptom duration, mo = 3 to 30<br>Intervention group = 295<br>No other characteristics reported.<br>Comparator group = 318<br>No other characteristics reported | Intervention: PRPi<br>N injections, dose, frequency (12 RCTs) = NR, range 2 to 8 mL, NR<br>Comparator: CS injection (12 RCTs)<br>N injections, dose, frequency = NR, range 8 to 80 mg, NR | Outcomes (measures): Pain (VAS), Composite of pain, function and alignment (AOFAS score), safety (adverse events)<br>Follow-up: 0.75 to 24 months |

| 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 |
|---|---|---|---|---|
| Trams et al. (2020)[28]<br>Poland<br>**Funding source:**<br>Centre of Postgraduate Medical Education Grant, grant number 501 to 1–007 to 18 to 20 | Primary studies eligible for this review: 3 RCTs of 83 included RCTs and NRS<br>Primary studies summarized in this report: 1 of the 3 eligible RCTs that were not included in the other SRs included in this report.<br>Sources and dates searched: The sources searched were PubMed, Embase, Cochrane Database of Systematic Reviews, and Clinicaltrials.gov from database with no search time frame specified (authors report only that the search was conducted in February 2020) | All eligible patients, N = 18<br>Patellar tendinopathy = 36<br>Intervention groups = 18<br>No other characteristics reported.<br>Comparator group = 18<br>No other characteristics reported | Intervention: PRPi<br>N injections, dose, frequency (1 RCT) = 2, NR, NR<br>Comparator: Saline injections<br>N injections, dose, frequency (1 RCT) = 2, NR, NR | Outcomes: Function (VISA); pain (VAS)<br>Follow-up: 6 months |
| Franchini et al. (2019)[29]<br>Italy<br>**Funding source:**<br>NR | Primary studies eligible for this review: 16 of 36 included RCTs<br>Primary studies summarized in this report: 4 of the 16 eligible RCTs that were not included in the other SRs included in this report.<br>Sources and dates searched: The sources searched were MEDLINE (through PUBMED), Embase, SCOPUS, OVID and Cochrane Library electronic databases from an unspecified time point to April 2018 | All eligible patients, N = 260<br>Plantar fasciitis = 260<br>Intervention groups = 120<br>Average age in years, range = 40.9 to 44.7<br>Male-female ratio, range = 5:10 to 7:8<br>Comparator groups = 140<br>Average age in years, range = 37.8 to 46.8<br>Male-female ratio = 4:11 to 27:33 | Intervention: PRPi<br>N injections, dose, frequency (4 RCTs) = 1, range 2 to 4 mL, NA<br>Comparator: Steroid injection (2 RCTs), saline injection (1 RCT), dry needling (1 RCT)<br>N injections, dose, frequency (1 RCT) = 1, range 2 to 4 mL (2 RCTs) NR (2 RCTs), NR | Outcomes: Function (FFI, AOFAS), NR (FAAM, VISA), pain (VAS)<br>Follow-up: Range 2 to 6 months |

AOFAS = American Orthopedic Foot and Ankle Society; d = day(s); EQ-VAS = EuroQoL visual analogue scale; FFI = Foot Function Index; HHS = Harris Hip Score; LR-PRPi = leucocyte-rich platelet-rich plasma injection; MA = meta-analysis; mg = milligram(s); mL = millilitre; mo = month(s); n/N = number(s); NA = not applicable; NI = not interpretable; NR = not reported; NRS = non-randomized study; PRPi = platelet-rich plasma injection; PT = physiotherapy;

R&D = research and development; RCT = randomized controlled trial; RoM = range of motion; SD = standard deviation; SF-12 = Short Form 12; SR = systematic review; VAS = visual analogue scale; VISA-A = Victorian Institute of Sports Assessment–Achilles; VISA-P = Victorian Institute of Sports Assessment–Patellar; wk = week(s); yr = year(s):

[a]Reported as 'Signe injection' i.e., not interpretable.

[b]Totals for sex do not add to overall patient totals as sex was not reported for some studies.

AOFAS: The AOFAS is scored from 0 to 100, with 100 representing no symptoms or impairment and lower scores representing increasing symptoms and impairment.[46]

EQ-VAS: The EQ-VAS is presented as a score from 0 to 100, with 100 representing best possible health and lower scores representing increasing symptoms and impairment.

FAAM: The FAAM is presented as a score from 0 to 100, with 100 representing no symptoms or impairment and lower scores representing increasing symptoms and impairment.[47]

FFI: The FFI is reported on a scale from 0 to 100, with 0 representing no symptoms or disability and higher scores representing increasing symptoms and disability.[48]

HHS: The HHS is presented as a score from 0 to 100, with 100 representing no symptoms or impairment and lower scores representing increasing symptoms and impairment.[49]

SF-12: The SF-12 is presented as a score from 0 to 100, with 100 representing best possible health and lower scores representing increasingly poor health.[50]

VAS: The VAS is generally scored from 0 to 10, with 0 representing no pain and 10 representing the worst possible pain.[51]

VISA, VISA-A, VISA-P: The VISA and VISA-P are scored using a numeric scale from 0 to 100, with 100 representing no symptoms and lower scores more deleterious symptoms.[45,52,53]

# Appendix 3: Critical Appraisal of Included Publications

Note that this appendix has not been copy-edited.

## Table 4: Strengths and Limitations of Overview of Systematic Reviews Using AMSTAR 2[20] With Additional Items

| Strengths | Limitations |
|---|---|
| **Irby 2023[21]** | |
| • A rationale for limitation of study design to SRs only was provided<br>• The search included > 2 relevant databases, search keywords were reported, and the search was completed within 24 months of the report being published<br>• Inclusion criteria described the components of PICOS<br>• Study selection and data abstraction were performed by > 1 reviewer<br>• Authors assessed overlap in primary studies across the included SRs with a corrected covered area assessment<br>• The AMSTAR tool was used to assess RoB for included SRs<br>• The qualitative synthesis approach was appropriate<br>• RoB was discussed in the interpretation of findings<br>• Funding and conflicts of interest were reported as 'none' | • There was no mention of a review protocol or an a priori development of review methods<br>• The comprehensiveness of the search strategy was unclear i.e., information on keywords, publication restrictions, consultation of experts (e.g., for search strategy development) and grey literature search were not provided<br>• A list of excluded studies was not provided<br>• Details of the intervention and comparator were not provided i.e., N injections, dose, frequency and interval(s) between injections<br>• Information on follow-up timing was NR<br>• Information on the quality of evidence within SRs (i.e., primary included studies) was not described<br>• There was no mention of heterogeneity across included SRs<br>• Sources of funding for included SRs were not described |

PICOS = population(s), intervention(s), comparator(s), outcome(s), study design(s); RoB = risk of bias; SR = systematic review

## Table 5: Strengths and Limitations of Systematic Reviews Using AMSTAR 2[20]

| Strengths | Limitations |
|---|---|
| **Masiello (2023)[22]** | |
| • A review protocol was registered with PROSPERO<br>• The search included > 2 relevant databases, relevant keywords were reported and the search was completed within 24 months of the report being published<br>• The search strategy was not limited by language and reference lists of included studies were searched<br>• Data abstraction was performed in duplicate<br>• RoB assessments were conducted in duplicate and informed by the Cochrane Handbook<br>• Methods for meta-analyses appeared to be appropriate<br>• The potential impact of RoB in individual studies on the results of the meta-analyses was discussed<br>• Review authors discussed RoB when interpreting the findings of the review<br>• Heterogeneity and publication bias were investigated as | • The review objectives described the population and intervention but was not clear about comparator(s), outcome(s) or study design(s) of interest<br>• There was no rationale provided for limiting the review to RCTs only<br>• The source(s) of funding to support the SR was not reported<br>• Consultation of experts to support search strategy development was not described<br>• The earliest date of the search time frame was not reported<br>• Study selection methods were not described<br>• Details of the population, intervention and comparator were not provided i.e., patient characteristics, mode of administration (comparator only), N injections, dose, frequency and interval(s) between injections<br>• Excluded studies were not listed<br>• A discussion of the findings of the assessments of heterogeneity |

| Strengths | Limitations |
|---|---|
| part of a GRADE assessment performed by the authors<br>• Authors were explicit concerning no conflicts of interest | and publication bias was not provided<br>• Sources of funding for included RCTs were not described |
| **Nuhmani (2023)[23]** | |
| • A protocol was registered with PROSPERO<br>• The inclusion criteria included the components of PICOS<br>• The search strategy was sufficient<br>• Study selection and data abstraction were performed by > 1 reviewer<br>• Two independent reviewers assessed the quality of included studies using the PEDRo scale<br>• Authors were explicit concerning no competing interests | • The source(s) of funding was reported only as 'Nil'<br>• There was no rationale provided for limiting the review to RCTs<br>• Excluded studies were not listed<br>• Data were abstracted by a single reviewer<br>• Intervention details were not provided i.e., N injections and dose<br>• Descriptions of some outcomes and measures were missing<br>• Outcomes were reported without specifying the follow-up timing<br>• Heterogeneity was mentioned as the reason that no MA was undertaken, but an explicit discussion of the observed heterogeneity was not reported |
| **Vithran (2023)[24]** | |
| • The inclusion criteria included the components of PICOS<br>• A protocol was registered with PROSPERO<br>• The search included > 2 relevant databases, relevant keywords were reported and the search was completed within 24 months of the report being published<br>• Study selection and data abstraction were performed by > 1 reviewer<br>• No information was provided on whether the quality assessments were performed by > 1 reviewer<br>• Methods for meta-analyses appeared to be appropriate<br>• Authors did not explicitly describe the potential impact of RoB on the results of the MA<br>• Authors described the presence of significant statistical heterogeneity for several outcomes and the use of a random-effects model to account for these<br>• An assessment of publication bias was reported<br>• Authors were explicit concerning no conflicts of interest and reported their sources of funding | • There was no rationale described for limiting the review to RCTs only<br>• Consultation of experts to support search strategy development was not described<br>• Duplicate data abstraction was not described<br>• Excluded studies were not listed<br>• Details of the comparator were not provided i.e., N injections, dose, frequency<br>• Studies were assessed for quality using the Jadad scale<br>• Authors conducted sensitivity analyses<br>• Authors did not explicitly address the potential impact of heterogeneity on the findings of the review<br>• No discussion of the impact of publication bias on the results of the review was reported |
| **Barman (2022)[25]** | |
| • The inclusion criteria included the components of PICOS<br>• A protocol was registered with PROSPERO<br>• The search included > 2 relevant databases, relevant keywords were reported and the search was completed within 24 months of the report being published<br>• Study selection and data abstraction were performed by > 1 reviewer<br>• Included studies were described in sufficient detail<br>• Two independent reviewers assessed included studies using the Cochrane Risk of Bias tool | • The rationale for selection of study designs was not made explicit<br>• Consultation of experts to support search strategy development was not described<br>• The earliest date of the search time frame was not reported<br>• Excluded studies were not listed<br>• Sources of funding for included primary studies were not described<br>• Authors conducted sensitivity analyses but did not explicitly describe the potential impact of RoB on the results of the MA<br>• RoB was not explicitly addressed in the interpretation of findings |

| Strengths | Limitations |
|---|---|
| • Methods for meta-analyses appeared to be appropriate<br>• Authors included a report of adverse events<br>• Conflicts of interest were reported as 'not applicable' and authors reported no source(s) of funding | • Heterogeneity was assessed but a discussion of the findings of that assessment was not provided<br>• There was no mention of an assessment of publication bias |
| **Migliorini (2021)[26]** | |
| • The inclusion criteria included the components of PICOS<br>• The search included > 2 relevant databases, relevant keywords were reported and the search was completed within 24 months of the report being published<br>• Study selection was performed by > 1 reviewer<br>• Data abstraction was performed by > 1 reviewer<br>• Two independent reviewers assessed included studies using the Cochrane Risk of Bias tool<br>• Methods for meta-analyses appeared to be appropriate<br>• Heterogeneity was accounted for in the MA i.e., random effects modelling was used where heterogeneity was high; there was some discussion of the impact of heterogeneity on the interpretability of the findings of the review<br>• The authors declared they had no conflicts of interest and no source(s) of external funding (though, any other e.g., internal, sources of funding were NR) | • There was no mention of a review protocol or a priori method<br>• The rationale for selection of study designs was not made explicit<br>• Consultation of experts to support search strategy development was not described<br>• The earliest date of the search time frame was not reported<br>• Excluded studies were not listed<br>• Details for some features of intervention and comparators were not provided i.e., N injections, dose, frequency<br>• Sources of funding for included primary studies not described<br>• There was no explicit assessment of the potential impact of RoB to the findings of the MA<br>• RoB was mentioned in the in the discussion and interpretation of findings, but was limited to a statement that the quality of all included studies was high<br>• There was no mention of an assessment of publication bias<br>• While authors declared they had no source(s) of external funding, any other (e.g., internal), sources of funding were NR |
| **Huang (2020)[27]** | |
| • The inclusion criteria included the components of PICOS<br>• A protocol was registered with PROSPERO<br>• The search included > 2 relevant databases, relevant keywords were reported and the search was completed within 24 months of the report being published<br>• Study selection was performed by > 1 reviewer<br>• Two independent reviewers assessed included studies using the Cochrane Risk of Bias tool<br>• Methods for meta-analyses appeared to be appropriate<br>• Sensitivity analyses were conducted to address the potential impact of RoB<br>• Authors explicitly addressed the potential for RoB in individual studies in the results of the review<br>• Authors assessed statistical heterogeneity and discussed the implications in the interpretation of findings<br>• Authors reported both sources of funding, including potential conflicts of interest<br>• Authors explicitly addressed the importance of MCID with regard to the primary outcomes<br>• Authors included a report of adverse events | • The rationale for limiting eligible study design to RCTs was not made explicit<br>• Consultation of experts to support search strategy development was not described<br>• The authors did not describe whether data abstraction was performed in duplicate<br>• Excluded studies were not listed<br>• Details for intervention and comparators were missing i.e., N injection(s), frequency<br>• Sources of funding for included primary studies were not described<br>• There was no mention of an assessment of publication bias |

| Strengths | Limitations |
|---|---|
| **Trams (2020)[28]** | |
| • The inclusion criteria included the components of PICOS<br>• A protocol was registered with PROSPERO<br>• Search keywords were reported<br>• Authors report use of the Cochrane Risk of Bias tool by > 1 reviewer<br>• Authors reported the source of funding for the review and claimed no conflicts of interest | • The rationale for limiting eligible study design to RCTs was not made explicit<br>• The dates of the search time frame were not reported<br>• Consultation of experts to support search strategy development was not described<br>• Study selection methods were NR<br>• The authors did not describe whether data abstraction was performed in duplicate<br>• Excluded studies were not listed<br>• Details of the population characteristics were NR<br>• Details for intervention and comparator were missing i.e., dose, frequency<br>• Sources of funding for included primary studies were not described<br>• The authors did not report methods for quantitative synthesis in sufficient detail<br>• Only a cursory mention of the possible impact of RoB and heterogeneity on the findings of the review was mentioned<br>• There was no mention of an assessment of publication bias |
| **Franchini (2018)[29]** | |
| • The inclusion criteria included the components of PICOS<br>• > 2 relevant databases were searched and search keywords were reported<br>• Study selection was performed by > 1 reviewer<br>• Data abstraction was performed by > 1 reviewer<br>• Authors report use of the Cochrane RoB tool by > 1 reviewer<br>• Methods for meta-analyses appeared to be appropriate<br>• Heterogeneity was assessed statistically in the MA and was discussed in the interpretation of findings<br>• Authors reported potential conflicts of interest | • There was no mention of a review protocol or a priori method<br>• The rationale for limiting eligible study design to RCTs was not made explicit<br>• The earliest date of the search time frame was not reported<br>• Consultation of experts to support search strategy development was not described<br>• Excluded studies were not listed<br>• Some outcomes were not described, with only outcome measures listed<br>• Sources of funding for primary studies were not described<br>• There was no explicit assessment of the potential impact of RoB in individual studies to the findings of the MA<br>• Authors discussed their findings of quality of evidence from a GRADE assessment, but did not explicitly address the potential impact of RoB on the findings of the review<br>• There was no mention of an assessment of publication bias<br>• Source(s) of funding were NR |

AMSTAR 2 = A MeaSurement Tool to Assess systematic Reviews 2; GRADE = Grading of Recommendations, Assessment, Development, and Evaluations; MA = meta-analysis; MCID = minimal clinically important difference; n/N = number(s); NR = not reported; PEDro = Physiotherapy Evidence Database; PICOS = population(s), intervention(s), comparator(s), outcome(s), study design(s); PROSPERO = International prospective register of systematic reviews; RCT = randomized controlled trial; RoB = risk of bias; SR = systematic review.

# Appendix 4: Main Study Findings

Note that this appendix has not been copy-edited.

## Table 6: Summary of Findings by Outcome — Function

| SR citation and data from included study or studies | Measure, summary statistic | N patients | Follow- up | Results | | Group difference |
|---|---|---|---|---|---|---|
| | | | | PRPi | Comparator | |
| **Achilles** | | | | | | |
| Irby et al.[21]<br>Findings from 1 SR (4 RCTs):<br>Zhang 2018 | VISA-P, NR | 170 | NR | NR | Saline: NR | Reported as no difference |
| **Knee** | | | | | | |
| Barman et al. (2022)[25]<br>Findings from 2 RCTs:<br>Dragoo 2014<br>Scott 2019 | **Dragoo 2014 (RCT)** | | | | | |
| | VISA-P, mean (SD) | 19 | 8 to 12 wk[a] | 66.4 (20.2) | DN: 52 (20.3) | Mean difference (95% CI), statistical significance = 14.40 (−3.10 to 31.90), NS |
| | | | 6 months[a] | 66.4 (20.2) | 52 (20.3) | Mean difference (95% CI), statistical significance = 14.40 (−4.88 to 33.68), NS |
| | **Scott 2019 (RCT)** | | | | | |

| SR citation and data from included study or studies | Measure, summary statistic | N patients | Follow- up | Results | | Group difference |
|---|---|---|---|---|---|---|
| | | | | PRPi | Comparator | |
| | VISA-P, mean (SD) | 38 | 8 to 12 wk[a] | 63 (22) | Saline: 69 (18) | Mean difference (95% CI), statistical significance = −6.00 (−18.78 to 6.78), NS |
| | | | 6 months[a] | 63 (22) | 69 (18) | Mean difference (95% CI), statistical significance = −6.00 (−18.78 to 6.78), NS |
| | | | 1 yr | 58 (29) | 80 (18) | Mean difference (95% CI), statistical significance = −22.00 (−37.35 to −6.65), SS (favours control) |
| Trams et al. (2020)[28]<br>Findings from 1 RCT:<br>Abate 2018 | VISA, mean (SD) | 36 | 6 months | 71.2 (12.3) | Saline: 63.4 (9.8) | Mean difference (95% CI), statistical significance = 7.80 (0.53 to 15.07), SS (favours PRPi) |
| **Plantar fasciitis** | | | | | | |
| Masiello et al. (2023)[22]<br>Findings from 1 RCT:<br>Ugurlar 2018 | FFI, NR | 79 | 36 months | NR | Steroid: NR | Reported as 'no difference' |

| SR citation and data from included study or studies | Measure, summary statistic | N patients | Follow- up | Results | | Group difference |
|---|---|---|---|---|---|---|
| | | | | PRPi | Comparator | |
| Franchini et al. (2018)[29]<br>Findings from 4 RCTs:<br>El Mallah 2017<br>Shekhar 2017<br>Homayouni 2016<br>Tank 2017 | **El Mallah 2017 (RCT)** | | | | | |
| | AOFAS, NR | 30 | 3 months | NR | DN: NR | Reported only as PRPi was more effective than DN |
| | **Shekhar 2017 (RCT)** | | | | | |
| | FFI, NR | 120 | 6 months | NR | Saline: NR | Reported only as PRPi was superior to saline |
| | **Homayouni 2016 (RCT)** | | | | | |
| | FAAM, NR | 30 | 2 months | NR | Steroid injection: NR | Reported only as no significant differences |
| | **Tank 2017 (RCT)** | | | | | |
| | FAAM, NR | 80 | 6 months | NR | Steroid injection: NR | Reported only as PRPi was more effective than steroid |

AOFAS = American Orthopedic Foot and Ankle Society; CI = confidence interval; DN = dry needling; FFI = Foot Function Index; mo = month(s); n/N = number(s); NR = not reported; NS = not significant; PRPi = platelet-rich plasma injection; RCT = randomized controlled trial; SD = standard deviation; SR = systematic review; SS = statistically significant; VISA = Victorian Institute of Sports Assessment; VISA-P = Victorian Institute of Sports Assessment–Patellar; wk = week(s).

[a]Results for the 8 to 12 week and 6 months time frames were reported as being the same for both groups across both studies (with the exception of the 95% CIs in the mean differences reported for Dragoo 2014); this may or may not be in error but could not be ascertained.

## Table 7: Summary of Findings by Outcome — Pain

| SR citation and data from included study/studies | Measure, summary statistic | N patients | Follow-up | Results | | Group difference |
|---|---|---|---|---|---|---|
| | | | | PRPi | Comparator | |
| **Hip** | | | | | | |
| Nuhmani et al. (2023)[23]<br>Findings from 1 RCT:<br>Jacobson 2016 | Pain score (measure NR) | 30 | Baseline | 31.4 | DN: 32.4 | Reported as "equally effective" |
| | | | 1wk | Postintervention (follow-up timing NSp) = 19.4<br>% improvement: 80 | Postintervention (follow-up timing NSp) = 15.2<br>% improvement = 93 | |
| | | | 2wk | | | |

| SR citation and data from included study/studies | Measure, summary statistic | N patients | Follow-up | Results | | Group difference |
|---|---|---|---|---|---|---|
| | | | | PRPi | Comparator | |
| Migliorini et al. (2021)[26]<br>MA of 2 primary studies:<br>Begkas 2020<br>De Goes 2016 | VAS, mean (SD) | 124 (hips) | 2 to 6 months | NR | Steroids: NR | Standardized mean difference (95% CI), statistical significance = −4.25 (−12.78 to 4.29), NS |
| **Knee** | | | | | | |
| Barman et al. (2022)[25]<br>Findings from 1 RCT and 1 NRS:<br>Dragoo 2014<br>Filardo 2010 | VAS, mean (SD) | Dragoo 2014 (RCT) | | | | |
| | | 19 | 8 to 12 wk | 1.7 (1.7) | DN: 2.3 (1.6) | Mean difference (95% CI), statistical significance = −0.60 (−2.03 to 0.83), NS |
| | | | 6 months | 1.7 (1.5) | 0.3 (0.5) | Mean difference (95% CI), statistical significance = 1.40 (0.31 to 2.49), SS (favours control) |
| | | Filardo 2010 (NRS) | | | | |
| | | 31 | 8 to 12 wk | 4.3 (1.7) | PT: 3.2 (2.4) | Mean difference (95% CI), statistical significance = 1.10 (−0.36 to 2.56), NS |
| | | | 6 months | 3.1 (1.2) | 3.7 (2.8) | Mean difference (95% CI), statistical significance = −0.60 (−2.10 to 0.90), NS |
| Trams et al. (2020)<br>Findings from 1 RCT:<br>Abate 2018 | VAS, mean (SD) | 36 | 6 months | 1 (0.6) | Saline: 1.7 (1.1) | Mean difference (95% CI), statistical significance = −0.70 (−1.28 to −0.12), SS (favours PRPi) |
| **Achilles** | | | | | | |
| Nuhmani et al. (2023)[23]<br>Findings from 1 RCT:<br>Abate 2019 | VAS, mean (SD) | 84 | Baseline | 5 (0.9) | DN: 4.9 (1.2) | Authors report that PRPi is slightly superior to DN, particularly in younger patients |

| SR citation and data from included study/studies | Measure, summary statistic | N patients | Follow-up | Results | | Group difference |
|---|---|---|---|---|---|---|
| | | | | PRPi | Comparator | |
| | | | 3mo | 4 (1.1) | 4 (1.1) | |
| | | | 6mo | 3.3 (1.5) | 3.3 (1.2) | |
| Vithran et al. (2023)[24]<br>MA of 3 primary studies:<br>Boesen 2017<br>Kearney 2013<br>Thermann 2020 | VAS, mean (SD) | 93 | 6wk | NR | Placebo: NR | Mean difference (95% CI), statistical significance = 6.75 (−6.12 to 19.62), NS |
| | | 93 | 3mo | | | Mean difference (95% CI), statistical significance = 11.30 (7.33 to 15.27), favours PRPi |
| | | 93 | 6mo | | | Mean difference (95% CI), statistical significance = 10.46 (−2.44 to 23.37), NS |
| | | 279 | Overall | | | Mean difference (95% CI), statistical significance = 11.74 (7.45 to 16.02), favours PRPi |
| **Plantar Fasciitis** | | | | | | |
| Masiello et al. (2023)[22]<br>Findings from 1 RCT:<br>Ugurlar 2018 | VAS, NR | 79 | 36 months | NR | Steroid: NR | Reported as 'no difference' |
| Huang et al. (2020)[27]<br>MA from 4 to 6 RCTs:<br>Acosto-Olivo 2017 (< 3mo data only)<br>Jain 2015<br>Jain 2018<br>Mahindra 2016 (< 3mo data only)<br>Tiwari 2013<br>Vahdatpour 2016 | VAS, mean (SD) | 500 | < 3 months | NR | CS injection: NR | Standardized mean difference (95% CI), statistical significance = 0.03 (−0.39 to 0.45), NS |

| SR citation and data from included study/studies | Measure, summary statistic | N patients | Follow-up | Results | | Group difference |
|---|---|---|---|---|---|---|
| | | | | PRPi | Comparator | |
| | | 218 | ≥ 3 months | NR | NR | Standardized mean difference (95% CI), statistical significance = −0.06 (−1.30 to 0.09), NS |
| Franchini et al. (2018)<br>Findings from 3 RCTs:<br>El Mallah 2017<br>Shekhar 2017<br>Tank 2017 | VAS, mean (SD) | **El Mallah 2017 (RCT)** | | | | |
| | | 30 | 3 months | NR | DN: NR | Reported only as PRPi was more effective than DN |
| | | **Shekhar 2017 (RCT)** | | | | |
| | | 120 | 6 months | NR | Saline: NR | Reported only as PRPi was superior to saline |
| | | **Tank 2017 (RCT)** | | | | |
| | | 80 | 3 months | 11.8 (5.1) | Steroid: 34.3 (7.8) | Mean difference (95% CI), statistical significance = −22.50 (−25.33 to −19.67), SS (favours PRPi) |
| | | | 6 months | 14.6 (6.9) | 30.2 (9.5) | Mean difference (95% CI), statistical significance = −15.60 (−19.21 to −11.99), SS (favours PRPi) |

CI = confidence interval; CS = corticosteroid; DN = dry needling; MA = meta-analysis; mo = month(s); n/N = number(s); NR = not reported; NRS = non-randomized study; NS = not significant; NSp = not specified; PRPi = platelet-rich plasma injection; PT = physiotherapy; RCT = randomized controlled trial; SD = standard deviation; SR = systematic review; SS = statistically significant; VAS = visual analogue scale; wk = week(s).

## Table 8: Summary of Findings by Outcome — Composite Outcomes

| SR citation and data from included study/studies | Measure, summary statistic | N patients | Follow-up | Results | | Group difference |
|---|---|---|---|---|---|---|
| | | | | PRPi | Comparator | |
| **Hip** | | | | | | |
| Migliorini et al. (2021)[26]<br>MA of 3 primary studies:<br>Begkas 2020 | HHS, mean (NR) | 124 (hips) | 2 to 6 months | NR | Steroids: NR | Standardized mean difference (95% CI), statistical significance = 0.51 |

| SR citation and data from included study/studies | Measure, summary statistic | N patients | Follow-up | Results | | Group difference |
|---|---|---|---|---|---|---|
| | | | | PRPi | Comparator | |
| De Goes 2016<br>Fitzpatrik 2018 | | | | | | (0.12 to 0.90), SS (favours PRPi) |
| **Achilles** | | | | | | |
| Vithran et al. (2023)[24]<br>MA of 6 to 8 primary studies:<br>De Vos 2010<br>De Jonge 2011<br>Kearney 2013<br>Krogh 2016 (no 6wk data)<br>Boesen 2017<br>Thermann 2020<br>VanderVlist 2020<br>Kearney 2021 (no 6wk data) | VISA-A, mean (NR) | 281 | 6wk | NR | Placebo: NR | Mean difference (95% CI), statistical significance = 1.92 (−0.54 to 4.38), NS |
| | | 532 | 3mo | | | Mean difference (95% CI), statistical significance = 0.20 (−2.65 to 3.05), NS |
| | | 519 | 6mo | | | Mean difference (95% CI) = 2.75 (−2.76 to 8.26), NS |
| | | 1,332 | Overall | | | Mean difference (95% CI), statistical significance = 1.20 (−0.94 to 3.34), NS |
| Nuhmani et al. (2023)[23]<br>Findings from 1 RCT:<br>Abate 2019 | VISA-A, mean (SD) | 84 | Baseline | 49.7 (8.8) | DN: 50.8 (9.5) | Authors conclude that PRPi is slightly superior to DN, particularly in younger patients |
| **Plantar Fasciitis** | | | | | | |
| Huang et al. (2020)[27]<br>MA from 3 to 5 RCTs:<br>Acosto-Olivo 2017 (< 3mo data only)<br>Jain 2015<br>Jain 2018 | AOFAS, mean (NR) | 356 | < 3 months | NR | CS injection: NR | Standardized mean difference (95% CI), statistical significance = 0.34 (−0.18 to 0.87), NS |

| SR citation and data from included study/studies | Measure, summary statistic | N patients | Follow-up | Results | | Group difference |
|---|---|---|---|---|---|---|
| | | | | PRPi | Comparator | |
| Mahindra 2016 (< 3mo data only)<br>Monoto 2014 | | | | | | |
| | | 252 | ≥ 3 months | NR | NR | Standardized mean difference (95% CI), statistical significance = 1.94 (0.61 to 3.28), SS (favours CS) |
| Franchini et al. (2018)<br>Findings from 1 RCT:<br>Tank 2017 | ***Tank 2017 (RCT)*** | | | | | |
| | VISA, NR | 80 | 6 months | NR | Steroid injection: NR | Reported only as PRPi was more effective than steroid |

AOFAS = American Orthopedic Foot and Ankle Society; CI = confidence interval; CS = corticosteroid; HHS = Harris Hip Score; MA = meta-analysis; mo = month(s); N = number; NR = not reported; NS = not significant; PRPi = platelet-rich plasma injection; RCT = randomized controlled trial; SD = standard deviation; SR = systematic review; SS = statistically significant; VISA = Victorian Institute of Sports Assessment; VISA-A = Victorian Institute of Sports Assessment–Achilles; wk = week(s).

## Table 9: Summary of Findings by Outcome — Return to Exercise/Sport

| SR citation and data from included study/studies | Measure, summary statistic | N patients | Follow-up | Results | | Group difference |
|---|---|---|---|---|---|---|
| | | | | PRPi | Comparator | |
| **Achilles** | | | | | | |
| Vithran et al. (2023)<br>MA of 4 RCTs:<br>De Vos 2010<br>De Jonge 2011<br>Boesen 2017<br>VanderVlist 2020 | Proportion of patients, n/N | 199 | 2 to 48 wk | 58/98 | Placebo: 54/101 | RR (95% CI), statistical significance = 1.11 (0.87 to 1.42), NS |

CI = confidence interval; MA = meta-analysis; n/N = number(s); NS = not significant; PRPi = platelet-rich plasma injection; RCT = randomized controlled trial; RR = risk ratio; SD = standard deviation; SR = systematic review; wk = week(s).

## Table 10: Summary of Findings by Outcome — Patient Satisfaction

| SR citation and data from included study/studies | Measure, summary statistic | N patients | Follow-up | Results | | Group difference |
|---|---|---|---|---|---|---|
| | | | | PRPi | Comparator | |
| **Achilles** | | | | | | |
| Vithran et al. (2023)<br>MA of 4 RCTs:<br>De Vos 2010<br>De Jonge 2011<br>Boesen 2017<br>VanderVlist 2020 | Patients satisfied, n/N | 222 | 2 to 48 wk | 63/110 | Placebo: 60/112 | RR (95% CI), statistical significance = 1.07 (0.84 to 1.35), NS |

CI = confidence interval; MA = meta-analysis; n/N = number(s); NS = not significant; PRPi = platelet-rich plasma injection; RCT = randomized controlled trial; RR = risk ratio; SR = systematic review; wk = week(s).

## Table 11: Summary of Findings by Outcome — Quality of Life

| SR citation and data from included study/studies | Measure, summary statistic | N patients | Follow- up | Results | | Group difference |
|---|---|---|---|---|---|---|
| | | | | PRPi | Comparator | |
| **Knee** | | | | | | |
| Barman et al. (2022)[25]<br>MA of 2 primary studies:<br>Dragoo 2014<br>Filardo 2010 | SF-12, EQ-VAS, mean (NR) | 52 | 8 to 12 wk | NR | DN, PT: NR | Mean difference (95% CI), statistical significance = −0.09 (−0.64 to 0.46), NS |
| | | 48 | 6 months | | | Mean difference (95% CI), statistical significance = 0.03 (−0.54 to 0.60), NS |

CI = confidence interval; DN = dry needling; EQ-VAS = EuroQOL visual analogue scale; MA = meta-analysis; mo = month(s); n/N = number(s); NR = not reported; NS = not significant; PRPi = platelet-rich plasma injection; PT = physiotherapy; SF-12 = short form 12; SR = systematic review; wk = week(s).

## Table 12: Summary of Findings by Outcome — Adverse Events

| SR citation | Primary studies | Adverse events | Patients affected, n (%) | | Group difference |
|---|---|---|---|---|---|
| | | | Intervention group | Comparator group | |
| **Knee** | | | | | |
| Barman et al. (2022)[25] | Scott 2019 | Serious adverse events | 0 (0) | 0 (0) | NR |
| | Dragoo 2014 | Any adverse event | 0 (0) | 0 (0) | |
| | Filardo 2010 | | | | |
| Huang et al. (2020)[27] | Aksahin 2012 | Any adverse event | 0 (0) | 0 (0) | NR |
| | Tiwari 2013 | | | | |

| SR citation | Primary studies | Adverse events | Patients affected, n (%) | | Group difference |
|---|---|---|---|---|---|
| | | | Intervention group | Comparator group | |
| | Say 2014 | | | | |
| | Jain 2015 | | | | |
| | Jain 2018 | | | | |

n/N = number(s); NR = not reported; SR = systematic review.

# Appendix 5: Overlap Between Included Systematic Reviews

## Table 13: Overlap in Relevant Primary Studies Between Included Systematic Reviews

| Primary study citation | Nuhmani 2023[23] | Masiello 2023[22] | Vithran 2023[24] | Barman 2022[25] | Migliorini 2021[26] | Huang 2020[27] | Trams 2020[28] | Franchini 2018[29] |
|---|---|---|---|---|---|---|---|---|
| **Hip** | | | | | | | | |
| Begkas 2020 | — | — | — | — | Yes | — | — | — |
| Thompson 2019 | — | — | — | — | Yes | — | — | — |
| Fitzpatrick 2018 | — | — | — | — | Yes | — | — | — |
| De Goes Ribeiro 2016 | — | — | — | — | Yes | — | — | — |
| Jacobson 2016 | Yes | — | — | — | — | — | — | — |
| **Knee** | | | | | | | | |
| Scott 2019 | — | Yes | — | Yes | — | — | Yes | — |
| Abate 2018 | — | — | — | | — | — | Yes | — |
| Dragoo 2014 | Yes | Yes | — | Yes | — | — | Yes | Yes |
| Filardo 2010 | — | — | — | Yes | — | — | — | — |
| **Achilles** | | | | | | | | |
| Kearney 2021 | — | — | Yes | — | — | — | — | — |
| Boesen 2020 | — | Yes | — | — | — | — | — | — |
| Thermann 2020 | — | — | Yes | — | — | — | — | — |
| VanderVlist 2020 | — | — | Yes | — | — | — | — | — |
| Abate 2019 | Yes | — | — | — | — | — | — | — |
| Boesen 2017 | — | Yes | Yes | — | — | — | — | Yes |
| Krogh 2016 | — | Yes | Yes | — | — | — | — | Yes |
| Kearney 2013 | — | — | Yes | — | — | — | — | Yes |

| Primary study citation | Nuhmani 2023[23] | Masiello 2023[22] | Vithran 2023[24] | Barman 2022[25] | Migliorini 2021[26] | Huang 2020[27] | Trams 2020[28] | Franchini 2018[29] |
|---|---|---|---|---|---|---|---|---|
| De Jonge 2011 | — | Yes | Yes | — | — | — | — | Yes |
| De Vos 2010 | — | Yes | Yes | — | — | — | — | — |
| **Plantar fasciitis** | | | | | | | | |
| Jain 2018 | — | — | — | — | — | Yes | — | — |
| Ugurlar 2018 | — | Yes | — | — | — | — | — | — |
| Acosta-Olivo 2017 | — | — | — | — | — | Yes | — | Yes |
| El Mallah 2017 | — | — | — | — | — | — | — | Yes |
| Shekhar 2017 | — | — | — | — | — | — | — | Yes |
| Tank 2017 | — | — | — | — | — | — | — | Yes |
| Homayoumi 2016 | — | — | — | — | — | — | — | Yes |
| Mahindra 2016 | — | — | — | — | — | Yes | — | Yes |
| Sherpy 2016 | — | — | — | — | — | Yes | — | Yes |
| Vahdatpour 2016 | — | — | — | — | — | Yes | — | Yes |
| Jain 2015 | — | — | — | — | — | Yes | — | Yes |
| Monto 2014 | — | Yes | — | — | — | Yes | — | Yes |
| Say 2014 | — | — | — | — | — | Yes | — | — |
| Shetty 2014 | — | — | — | — | — | Yes | — | — |
| Tiwari and Bhargava 2013 | — | — | — | — | — | Yes | — | Yes |
| Aksahin 2012 | — | — | — | — | — | Yes | — | — |
| Omar 2012 | — | — | — | — | — | Yes | — | — |

# Appendix 6: References of Potential Interest

## Previous CADTH Reports

### *PRPI for Indications Other Than Chronic Tendinopathies of the Lower Extremities*

Platelet-rich plasma injections for wound healing and tissue rejuvenation: A review of clinical effectiveness, cost-effectiveness and guidelines. *(CADTH Rapid response report: summary with critical appraisal).* Ottawa (ON): CADTH; 2017: https://www.cadth.ca/platelet-rich-plasma-injections-wound-healing-and-tissue-rejuvenation-review-clinical-effectiveness

Platelet rich plasma lumbar disc injections for lower back pain: Clinical effectiveness, safety, and guidelines. *(CADTH Rapid response report: summary of abstracts)*. Ottawa (ON): CADTH; 2014: https://www.cadth.ca/sites/default/files/pdf/htis/mar-2014/RB0649%20Platelet%20Rich%20Plasma%20Final.pdf

## Review Articles

### *Narrative Reviews (i.e., No Systematic Review Method) of Relevance*

Sneed D, Wong C. Platelet-rich plasma injections as a treatment for Achilles tendinopathy and plantar fasciitis in athletes. *PM R.* 2023;10.1002/pmrj.12965. PubMed

Hulsopple C. Musculoskeletal therapies: Musculoskeletal injection therapy. *FP Essent*. 2018;470:21-26. PubMed

## Additional References

### *Methods Review Describing Statistical Challenges in PRPi Research*

Xu AL, Ortiz-Babilonia C, Gupta A, Rogers D, Aiyer AA, Vulcano E. The statistical fragility of platelet-rich plasma as treatment for chronic noninsertional achilles tendinopathy: A systematic review and meta-analysis. *Foot Ankle Orthop*. 2022;7(3):24730114221119758. PubMed