



Systematic Review of the Literature

The effectiveness of injection of steroid to the Hip as a form of interventional pain management

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Abbreviations

The following abbreviations are used in this report and are collated here for readers convenience

Abbreviation		Abbreviation	
AB	Autologous blood	PRP	Platelet rich plasma
CI	Confidence interval	RCT	Randomised controlled trial
CSI	Corticosteroid injections	ROM	Range of movement
ESWT	Extracorporeal shock wave therapy	RR	Risk Ratio /Relative Risk
FAI	Femora-acetabular impingement	RSWT	Radial shock wave therapy
GTPS	Greater trochanter pain syndrome	SIGN	Scottish Intercollegiate Guidelines Network
ITB	Iliotibial band syndrome	SMD	Standard mean difference
MA	Meta-analysis	SWT	Shock wave therapy
MPL	methylprednisolone	SR	Systematic review
NSAIDs	Non-Steroidal anti-Inflammatory drugs	TB	Trochanteric bursitis
NRS	Numerical rating scale	US	Ultrasound
OA	Osteoarthritis	VAS	Visual Analogue Scale
OMERA	Outcome measures in Rheumatology		
CT-	Clinical Trials - Osteoarthritis Research		
OARSI	Society International		
PICO	Population, Intervention, Comparator, Outcome		
PLA2	Phospholipase A2		
	Quality Ratings		
AQ	Acceptable Quality	LQ	Low Quality
CS	Can't say	NA	Not Applicable
HQ	High Quality	R	Reject (Unacceptable Quality)
QS	Quality of Study		

EXECUTIVE SUMMARY

<p>Objective of the Review</p>	<p>The objective of this systematic review is to synthesise the evidence related to the effectiveness of injection of steroid to the hip as a form of interventional pain management.</p> <p>In order to review the evidence this review aims to answer the following research questions</p> <ol style="list-style-type: none"> 1. What is the evidence for the effectiveness of steroid injections into the hip in relieving pain and/or in improving functional outcomes in patients with pain? 2. What is the evidence for the safety of steroid injections into hip?
<p>Evidence sourced</p>	<p>The search yielded 1535 articles. After scrutiny, 1523 articles were excluded as duplicates or failing to meet the inclusion criteria leaving 12 studies for inclusion in this review including 10 systematic reviews (SRs) and 2 randomised controlled trials (RCTs).</p>
<p>What is the evidence for the effectiveness of steroid injections into the hip in relieving pain and/or in improving functional outcomes in patients with pain?</p>	<p>Hip Osteoarthritis</p> <p>The evidence indicates that intra-articular steroid injection to the hip joint is effective in reducing pain and improving function in the short term (<8 weeks) in patients with hip osteoarthritis. They were not effective in reducing pain and improving function in the longer term (>8 weeks) <i>Level A recommendation based on 1 x HQ SR (McCabe et al., 2016) and 3 x LQ SRs (Kruse 2008, Peterson and Holder 2010, Hirsch et al., 2013)</i></p> <p>The evidence indicates that the effectiveness of intra-articular steroid injection to the hip joint was not related to radiographic grade of osteoarthritis and clinical or sonographic evidence of inflammation or synovial hypertrophy <i>Level B recommendation based on 1 x LQ SR (Hirsch et al., 2013)</i></p> <p>The evidence indicates that the effectiveness of intra-articular steroid injection to the hip joint was greater for 80 mg MPL than MPL 40mg but did not appear to be related to the volume of injectate used. <i>Level B recommendation based on 1 x LQ SR (Chandrasekaran et al., 2015)</i></p> <p>Greater Trochanter Pain Syndrome</p> <p>The evidence indicates that steroid injection to the hip is effective in reducing pain and improving function in the short term (up to 12 weeks) in patients with Greater Trochanter pain syndrome. They were not effective in reducing pain and improving function in the longer term (> 12 weeks) <i>Level A recommendation based on 2 x AQ SR (Barratt et al., 2016, DelBuono et al., 2012)</i></p>
<p>What is the evidence for the safety of steroid injections into the hip</p>	<p>Hip Osteoarthritis</p> <p>Minor complications associated with intra-articular steroid injections into the hip are not uncommon but rarely require significant medical attention. Whilst serious complications are rare, the hip joint appears susceptible to conditions such as calcifications and necrosis of the femoral head. Increased risk appears related to technique and repeated injections. <i>Level A recommendation</i></p>

	<p>Greater Trochanter Pain Syndrome</p> <p>Minor complications associated with steroid injections into the hip for Greater Trochanter pain syndrome are not uncommon but rarely require significant medical attention. <i>Level B recommendation</i></p>
<p>What is the evidence for differences in effectiveness if imaging is used?</p>	<p>Hip Osteoarthritis</p> <p>The evidence indicates that the effectiveness of intra-articular steroid injection to the hip joint was not related to the type of image guidance used. <i>Level B recommendation based on 1 x LQ SR (Hirsch et al., 2013)</i></p> <p>Greater Trochanter Pain Syndrome</p> <p>The evidence indicates that fluoroscopically guided steroid injections to the hip were no more effective than traditional bedside injection in reducing pain in patients with Greater Trochanter pain syndrome. <i>Level B recommendation based on 1 x AQ SR (Lustenberger et al., 2011)</i></p>
<p>Does the evidence report any information about cost effectiveness?</p>	<p>This review found no evidence related to the economic analysis of intra-articular steroid injections for hip osteoarthritis or of steroid injections for Greater Trochanter Pain Syndrome.</p>
<p>Compared to 2005 Recommendations</p>	<p>The recommendations from this review do not significantly change the findings from the previous 2005 review</p>

1. Background

1.1 Objective of this Review

The objective of this review is to synthesise the evidence related to the effectiveness of injection of steroid to the hip as a form of interventional pain management. This review will carry out a systematic review of the best available research evidence.

This review aims to answer the following research questions:

- a) What is the evidence for the effectiveness of steroid injections in patients with hip pain?
- b) What is the evidence for the effectiveness of steroid injections in improving functional outcomes in patients with hip pain?
- c) What is the evidence for the safety of steroid injections with or without local anaesthetic in patients with hip pain?

1.2 Description of the Intervention

Hip pain can present for a number of reasons. The most common sources of hip pain include the hip joint, usually secondary to osteoarthritis, and greater trochanter pain syndrome, including trochanteric bursitis.

Hip Joint Osteoarthritis

Osteoarthritis (OA) is the most common form of joint disease and the leading cause of pain in elderly people (da Costa et al., 2016). The hip joint is the second most common site of OA in the elderly (after the knee) (Felson 1990), with the reported prevalence of primary hip OA on radiographs ranging from 0.9% to 27.0% in different populations (Dagenais et al., 2009). The most consistently reported risk factors include age, genetics, congenital disorders of the hip joint, obesity, occupational and sporting related overload of the hip joint and joint injuries.

OA is generally defined as frequent joint pain and structural alterations on radiography. Symptoms associated with osteoarthritis result in increased physical and walking disability, which in turn increase the risk of all-cause mortality

OA is a condition that represents a pathological imbalance of degenerative and regenerative processes of joint structures. The pathologic process of OA begins in the articular cartilage, but ultimately the disease affects the whole joint, including cartilage, subchondral bone, synovium and periarticular soft tissues (Goldring and Goldring 2007). OA can either be a consequence of an abnormal mechanical load on a healthy joint or of a normal mechanical pressure on unhealthy cartilage tissue (Nuki and Salter 2007).

OA is not considered a classic inflammatory arthropathy due to the lack of systemic manifestations of inflammation, however, it is associated with signs and symptoms of inflammation including joint pain, swelling and stiffness. Synovial inflammation is a factor that is likely to contribute to deregulation of chondrocyte function, leading to an imbalance between the catabolic and anabolic activities of the chondrocyte in remodelling the cartilage extracellular matrix (Loeser et al., 2012).

Greater trochanter pain syndrome

The most common form of bursitis around the hip is trochanteric bursitis (TB), which as the name suggests involves inflammation in one or more of the several peritrochanteric bursae. However beneath the area where pain is perceived, several anatomic structures lie, including muscles, tendons, and entheses, in which imaging studies have shown abnormalities that appear to correlate better with the syndrome than bursal pathology. Given the irregular relationship between clinical symptoms and bursal pathology, authors have suggested the condition is best termed “greater trochanter pain syndrome.” (GTPS) (Shbeeb and Matteson 1996) An association between trochanteric bursitis syndrome and musculoskeletal abnormalities such as leg length discrepancy, iliotibial band contracture, lumbar spondylosis, and hip osteoarthritis has often been mentioned. However, none of these associations has been validly assessed.

TB/GTPS is almost always diagnosed clinically after exclusion of lumbar pathology such as spinal stenosis, spondylosis, and radiculopathy, hip conditions such as osteoarthritis, osteonecrosis, and stress fracture, as well as local processes such as soft tissue infection and bone or soft tissue tumors. The key diagnostic findings include; 1) lateral hip pain; 2) tenderness about the greater trochanter; 3) pain at the extremes of rotation, abduction, or adduction, especially a positive Patrick-fabere test; 4) pain on strong contraction of hip abductors; and 5) pseudoradiculopathy, mainly pain radiating down the lateral aspect of the thigh (Rasmussen and Fano 1985). Although the sensitivity, specificity, and predictive value have not been established.

Use of Steroid Injections

How steroid injections work in the management of pain remains controversial. Steroids have an anti-inflammatory effect, inhibiting fibroblast proliferation, angiogenesis, and formation of granulation tissue. They also interfere with collagen precursor ground substance sulfation and collagen repair. This inhibition occurs in specific leukocyte functions, including leukocyte aggregation at inflammatory sites, prevention of degranulation of granulocytes, mast cells, and macrophages, and stabilization of lysosomal and other membranes (Di Rosa et al., 1986). Corticosteroids also inhibit PLA2 activity, therefore interrupting the arachidonic acid cascade. It has also been shown that local application of cortisone blocks transmission in normal nociceptive C-fibres, potentially blocking nociceptive nerves in the manner of local anaesthetics.

Several different steroid preparations may be used, with or without local anaesthetic or normal saline to increase the volume of the injectate. Typical steroids used include methylprednisolone acetate, betamethasone acetate/propionate, and triamcinolone acetate. The benefits of adding a local anaesthetic include potential immediate pain relief for the patient which provides feedback to the practitioner that the steroid solution is near the presumed site of pathology

2. Methodology

<p>2.1 Review question</p>	<p>What is the effectiveness of injection of steroid in patients with hip pain?</p>								
<p>2.2 Methods</p>	<p>A systematic review of published research literature was undertaken to provide a synthesis of the currently available research evidence related to the effectiveness of steroid injections with or without local anaesthetic in patients with hip pain as a form of interventional pain management. A systematic and rigorous search strategy was developed to locate all published and accessible research evidence. The evidence base for this review included research evidence from existing systematic reviews, meta-analyses, and high-level primary research (randomised controlled trials, prospective cohort studies). Where no systematic reviews, randomised controlled trials, or prospective cohort studies were located then other primary study designs (excluding commentary /expert opinion) were considered.</p>								
<p>2.3 Search strategy</p>	<p>The search was developed using a standard PICO structure (shown in Table 1). Only English articles published, using human participants, which were accessible in full text were included.</p> <p style="text-align: center;">Table 1: Criteria for considering studies in the review</p> <table border="1" style="margin-left: auto; margin-right: auto;"> <tr> <td style="background-color: #cccccc;">Population</td> <td>Humans</td> </tr> <tr> <td style="background-color: #cccccc;">Intervention</td> <td>Steroid injection with or without local anaesthetic for patients with elbow pain (medial or lateral epicondyle) as a form of interventional pain management</td> </tr> <tr> <td style="background-color: #cccccc;">Comparator</td> <td>Any active treatment or placebo.</td> </tr> <tr> <td style="background-color: #cccccc;">Outcomes</td> <td> <ul style="list-style-type: none"> • Pain-related primary outcome; • Functional outcomes (range of motion, reduction of disability, return to work, quality of life) • Safety and Risk • Relationship to Imaging • Best Practice recommendations • Cost effectiveness </td> </tr> </table> <p>A combination of search terms (shown in Table 2) were used to identify and retrieve articles in the following databases:</p> <ul style="list-style-type: none"> ○ OVID • EMBASE, • MEDLINE, • AMED, ○ ICONDA, ○ CINAHL, ○ PubMed, ○ Pre-Medline, ○ The Cochrane Library, ○ Scopus, ○ TRIP database 	Population	Humans	Intervention	Steroid injection with or without local anaesthetic for patients with elbow pain (medial or lateral epicondyle) as a form of interventional pain management	Comparator	Any active treatment or placebo.	Outcomes	<ul style="list-style-type: none"> • Pain-related primary outcome; • Functional outcomes (range of motion, reduction of disability, return to work, quality of life) • Safety and Risk • Relationship to Imaging • Best Practice recommendations • Cost effectiveness
Population	Humans								
Intervention	Steroid injection with or without local anaesthetic for patients with elbow pain (medial or lateral epicondyle) as a form of interventional pain management								
Comparator	Any active treatment or placebo.								
Outcomes	<ul style="list-style-type: none"> • Pain-related primary outcome; • Functional outcomes (range of motion, reduction of disability, return to work, quality of life) • Safety and Risk • Relationship to Imaging • Best Practice recommendations • Cost effectiveness 								

Table 2: Search terms for the review

Search term 1	Search terms 2	Search terms 3	Search terms 4
• Pain	• Injections	• Hip joint	<ul style="list-style-type: none"> • Steroid • Betamethasone • Dexamethasone • Fluocortolone • Methylprednisolone • Paramethasone • Prednisolone • Prednisone • Triamcinolone • Hydrocortisone • Cortisone • Methandrostenolone • Stanozolol • Methenolone • Oxymetholone • Oxandrolone • Nandrolone • Diflucortolone • Fluprednisolone

The titles and abstracts identified from the above search strategy were assessed for eligibility by the ICAHE researchers. Full-text copies of eligible articles were retrieved for full examination. Reference lists of included full-text articles were searched for relevant literature not located through database searching.

Inclusion Criteria

- Study types: systematic reviews, all primary research designs (randomised controlled trials (RCTs), cohort studies (prospective or retrospective), case studies or case series.
- Participants: patients with hip pain
- Intervention: steroid injections with or without local anaesthetic
- Controls: any active treatment or placebo, or no intervention control
- Outcomes: pain relief (primary) functional outcomes, safety, and risk (secondary)
- Publication criteria – English language, full text available, in peer reviewed journal

Exclusion criteria

- Studies only available in abstract form e.g. conference presentations
- Grey literature and no-English language material
- Studies involving healthy volunteers or experimentally induced pain

**2.4
Study Selection**

2.5 Critical Appraisal

The SIGN (Scottish Intercollegiate Guidelines Network) checklist specific to the study design of the included studies was used to assess the methodological quality of the included studies. The SIGN checklist asks a number of questions with yes, no, can't say or not applicable as responses with the appraiser giving an overall rating of quality, based on the responses to questions of either high quality (++), acceptable (+), low quality (-) or unacceptable. As there is no SIGN Checklist for case studies these study designs will not be quality scored. Appendix 1 contains a copy of the SIGN checklists utilized in this study.

2.6 Data Extraction

Data were extracted from the identified publications using a data extraction tool which was specifically developed for this review. The following information were extracted from individual studies:

- Evidence source (Author, date, country)
- Level of evidence
- Characteristics of participants
- Interventions
- Outcome measures
- Results

For this review the studies that met the inclusion criteria were assessed for internal validity using the Scottish Intercollegiate Guidelines network (SIGN) Checklist for the relevant study design. Each study was graded for overall methodological quality using the SIGN Levels of evidence model

**2.7
Data Synthesis**

As described, for this review each study was graded for overall methodological quality using the SIGN checklist specific to the study design of the included studies.

Recommendations from the literature were made and scored according to a modification of the SIGN Evidence Grading matrix (see Table 3). The modification was to add levels 1 and 2 to differentiate between the 1+ and 1-, 2+ and 2- levels of evidence.

Table 3: Modified SIGN Evidence Grading Matrix

Levels of scientific evidence	
1++	High-quality meta-analyses, high-quality systematic reviews of clinical trials with very little risk of bias
1+	Well-conducted meta-analyses, systematic review of clinical trials or well-conducted clinical trials with low risk of bias
1	Meta-analyses, systematic review of clinical trials or clinical trials with a moderate (acceptable) level risk of bias.
1-	Meta-analyses, systematic reviews of clinical trials or clinical trials with high risk of bias.
2++	High-quality systematic reviews of cohort or case and control studies; cohort or case and control studies with very low risk of bias and high probability of establishing a causal relationship
2+	Well-conducted cohort or case and control studies with low risk of bias and moderate probability of establishing a causal relationship
2	Cohort or case and control studies with moderate risk of bias and potential risk that the relationship is not causal.
2-	Cohort or case and control studies with high risk of bias and significant risk that the relationship is not causal.
3	Non-analytical studies, such as case reports and case series.
4	Expert opinion.

To standardise the strengths of recommendations from the extensive literature used for this review a structured system was developed to incorporate a number of quality measures. Four measures were selected as important variables for the assessment of strength of recommendations from the primary and secondary research sources. These were

- a) Combination of data via Meta-analysis
- b) Quality of Systematic review/Trials
- c) Number of RCTs
- d) Consistency of the evidence

A scoring system was developed, based on a 0 and 1 score for each of these variables.

- 1. Combination of data via Meta-analysis: Yes = 1, No = 0
- 1. Quality of Systematic review: HQ/AQ (+) =1, LQ(0)/R = 0
- 2. Number of RCTs: ≥ 5 RCTs = 1, < 5 =0
- 3. Consistency: $\geq 75\%$ agreement = 1, $< 75\%$ agreement = 0

**2.8
Grades of
Recommendation**

This allowed for a maximum potentials core of 4 and a minimum score of 0, which reflected a measure of the evidence strength across a range of studies. The resultant score was transferred to the SIGN Evidence Grading matrix

Total Score	SIGN Evidence Grading matrix score
4	1++
3	1+
2	1
1/0	1-

Final recommendations were graded according to the Scottish Intercollegiate Guidelines network (SIGN) Grades of Recommendations (Table 4)

Table 4: Scottish Intercollegiate Guidelines network (SIGN) Grades of Recommendations

Grades of Recommendations	
A	At least one meta-analysis, systematic review or clinical trial classified as 1++ and directly applicable to the target population of the guideline, or a volume of scientific evidence comprising studies classified as 1+ and which are highly consistent with each other.
B	A body of scientific evidence comprising studies classified as 2++, directly applicable to the target population of the guideline and highly consistent with each other, or scientific evidence extrapolated from studies classified as 1++ or 1+.
C	A body of scientific evidence comprising studies classified as 2+, directly applicable to the target population of the guideline and highly consistent with each other, or scientific evidence extrapolated from studies classified as 2++.
D	Level 3 or 4 scientific evidence, or scientific evidence extrapolated from studies classified as 2+

3. Results

3.1 Evidence Sources

The search yielded 1535 articles; following removal of duplicates 164 articles were identified for screening of title and abstract. After scrutiny 152 articles were excluded for failing to meet the inclusion criteria (shown in Figure 1), leaving 12 studies for inclusion in this review. Figure 1 illustrates the process involved in study selection.

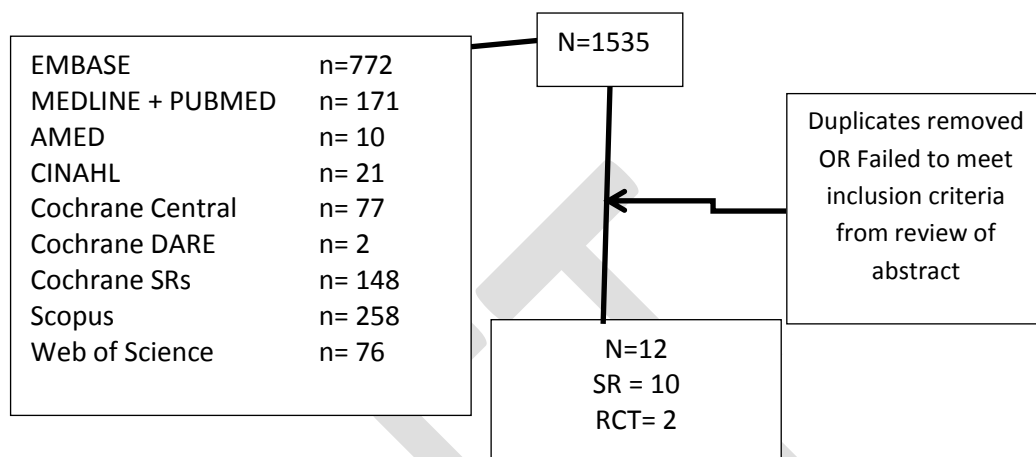


Figure 1: Flow chart of search results

The overall quality of the studies included in this review ranged from high quality to low quality.

	N=	HQ(++)	AQ(+)	LQ(-)	R(0)
Systematic reviews	10	1	3	4	2
RCTs	2	0	2	0	0

Appendices 2 and 5 present the critical appraisal scores for the systematic reviews and randomised controlled trials included in this review

Systematic reviews

- A) Studies did not address the potential for publication bias in reporting their reviews.
- B) Excluded studies were not listed
- C) Reviews often failed to differentiate between primary and secondary outcomes when synthesising their findings. Most systematic reviews used pain as a primary outcome and functional disability, etc, as secondary outcomes, but failed to differentiate between the two when synthesising the study findings in their reviews.
- D) Systematic Reviews often failed to define the specific pathology involved.

3.2 Quality of the Evidence

Randomised controlled trials

- A) The studies often failed to ensure that the only difference between the two groups (Intervention vs control) was the treatment under investigation. With the small numbers reported in the RCTs it was difficult to ensure that the effect of confounders was dealt with. This was particularly important when considering the effect of secondary outcomes. Studies rarely controlled for the patient's involvement in co-interventions such as exercise/medication etc.
- B) Subjects and investigators were rarely blinded to the intervention involved.
- C) Clinical studies often failed to define the specific pathology involved.
- D) Clinical studies often failed to consider the clinical spectrum of presentations to ensure homogeneity of subjects ie acute to chronic, severe to mild

DRAFT

Systematic reviews

A total of 10 systematic reviews were found in this review that investigated the effectiveness of steroid injections as a pain management intervention for the hip. These systematic reviews appraised 12 RCTs. Appendix 3 presents the findings from the systematic reviews included in this review. Appendix 4 presents the studies included in these systematic reviews.

Randomised controlled trials

A total of 2 RCTs that were not included in the 10 systematic reviews were identified in this review.

Hip OA

Systematic Reviews

Zhang et al., 2007/2010

Zhang et al., (2007) presented an umbrella review appraising the existing treatment guidelines and systematic review of current research evidence into the evidence for the management of hip and knee OA. They found 14 guidelines that did not separate hip and knee, eight were specific for knee but only one was specific for the hip joint. Unfortunately whilst the meta-analysis calculated a significant effect from Intra articular corticosteroid the review by Zhang et al., (2007) failed to differentiate between hip and knee OA so the findings are not relevant to this review. An evidence update from the same authors in 2010 (Zhang et al., 2010) suffered similar biases. Zhang et al., (2007) and Zhang et al., (2010) were not critically appraised or assessed for level of evidence due to the lack of relevance.

Kruse 2008

Kruse (2008) (QS:LQ(-)) presented a systematic review into the effectiveness of intraarticular steroid injection for osteoarthritis of the hip. They included RCT, longitudinal clinical outcome studies, retrospective analysis studies, review articles, and case reports published from 1955 to 2008.

They identified 8 trials that fulfilled their criteria of which only 4 were RCTs (Lambert et al., 2007, Kullenberg et al., 2004, Qvistgaard et al., 2006, Flanagan et al., 1988). The authors concluded that despite a paucity of RCT evidence the available evidence indicated a short-term reduction of pain with steroid injection and is indicated for patients refractory to non-pharmacologic or analgesic and NSAID therapy. The use of radiologic-guidance was recommended and, with proper sterile technique, the risk of adverse outcomes was very low.

Study	QS	Conclusions	Level of Evidence
Kruse (2008)	LQ(-)	Short term reduction in pain with intra-articular steroid injection for OA of the hip	1-

Peterson and Holder 2010

Peterson and Holder (2010) (QS:LQ(-)) undertook a systematic review into the evidence related to the use of therapeutic injections into the peripheral joints, which included the hip joint. This review included systematic reviews, meta-analyses and RCTs and excluded expert opinion, cohort studies and guidelines. The review failed to quality appraise the studies that were included. The review identified three prospective, double-blinded RCTs (Qvistgaard et al., 2006, Kullenberg et al., 2004, Lambert et al., 2007). They concluded that based on the three studies reviewed, it appears that steroid injections into the hip provided short-term improvement in pain and function (2–3 months), particularly for night pain, but that they were not effective for long-term pain relief.

Study	QS	Conclusions	Level of Evidence
Peterson and Holder (2010)	LQ(-)	Steroid injections provide short-term improvement in pain and function (2–3 months) in patients with hip OA, particularly for night pain, but that they are not effective for long-term pain relief.	1-

Hirsch et al., 2013

Hirsch et al., (2013) (QS:LQ(-)) presented a systematic review into the factors affecting pain relief from intra-articular steroid injections in patients with hip and knee osteoarthritis. The included both RCTs and observational cohort studies with no date limits on their search strategy. They identified 8 studies that specifically looked at the hip joint, all of which used image guidance, either fluoroscopic guidance (n=5) or ultrasound guidance (n=3). Five of the studies were clinical trials (Lambert et al., 2007, Flanagan et al., 1988, Young et al., 2012, Atchia et al., 2011, Qvistgaard et al., 2006) and 3 were observational studies (Deshmukh et al., 2011, Plant et al., 1997, Robinson et al., 2007).

The authors concluded that there were no factors that the evidence supported as a potential predictor of response to steroid injection to the hip, including radiographic grade and clinical or sonographic evidence of inflammation or synovial hypertrophy.

Study	QS	Conclusions	Level of Evidence
Hirsch et al., (2013)	LQ(-)	No factors appear as potential predictor of response to steroid injection to the hip, including radiographic grade and clinical or sonographic evidence of inflammation or synovial hypertrophy.	1-

Chandrasekaran et al., 2015

Chandrasekaran et al., (2015) (QS:LQ(-)) undertook a systematic review into the evidence for the use of intra-articular steroid or hyaluronic acid injection in the hip for the treatment of osteoarthritis or Femora-acetabular Impingement (FAI). They included case series, RCTs or meta-analysis that were specific to patients with osteoarthritis, FAI or labral tears.

They identified 26 articles related to the efficacy of steroid injections for hip osteoarthritis of which 2 were RCTs, (Kullenberg et al., 2004; Young et al., 2012) 11 were non-RCTs and 13 were retrospective studies.

The authors concluded that following intra-articular steroid injection for hip osteoarthritis was a significant reduction in pain and improvement in hip scores for up to 12 weeks, that 80 mg MPL produced a sustained improvement in pain, stiffness and function compared with 40 mg MPL, but that volume of injection alone did not affect efficacy.

Study	QS	Conclusions	Level of Evidence
Chandrasekaran et al., (2015)	LQ(-)	Intra-articular steroid injection for hip OA was a significant reduction in pain and improvement in hip scores for up to 12 weeks,	1-
		80 mg MPL produces a sustained improvement in pain, stiffness and function compared with 40 mg MPL	1-
		The volume of injection alone did not affect efficacy.	1-

McCabe et al., 2016

McCabe et al., (2016) (QS:HQ(-++)) presented a systematic review/meta-analysis into the efficacy of intra-articular steroids in hip osteoarthritis. This review included RCTs that assessed the use of intra-articular steroid injections in patients with painful hip osteoarthritis that was diagnosed on the presence of hip pain and radiological evidence of osteoarthritis. All studies had to include an intervention group which received a steroid injection and a control group who received a placebo (sham injection, normal saline or local anaesthetic intra-articular injection). The prime focus of the review was the effect on self-reported pain, however data was also reviewed for the secondary outcome of function.

They identified 5 RCTs (Kullenberg et al., 2004, Lambert et al., 2007, Qvistgaard et al., 2006, Atchia et al., 2011, Flanagan et al., 1988), all of which reported on small sample sizes (< 101). All 5 studies reported a reduction in pain at 3-4 weeks post-injection compared to control, with a large treatment effect size at 1 week post-injection which declined thereafter. A significant (moderate effect size) reduction in pain was reported in two trials up to 8 weeks following steroid injection. Pooled results of two trials (n = 90) showed an increased likelihood of meeting the Outcome measures in Rheumatology Clinical Trials - Osteoarthritis Research Society International (OMERACT- OARSI) response criteria at 8 weeks following steroid injection, odds ratio 7.8 (95% confidence interval (CI): 2.7-22.8). The number needed to treat to achieve one OMERACT-OARSI responder at 8 weeks post-injection was 2.4 (95% CI: 1.7-4.2).

Figure 2: Pooled results of McCabe et al., 2016

Study	QS	Conclusions	Level of Evidence
McCabe et al., (2016)	HQ(++)	Intra-articular steroid injection for hip OA was a significant reduction in pain and improvement in hip scores in the short term (up to 8 weeks)	1+

Greater Trochanter pain syndrome

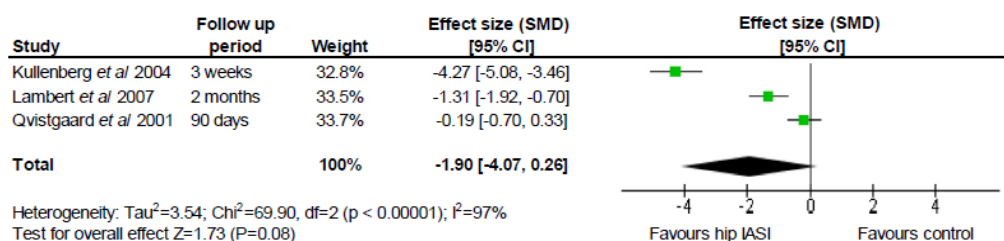
Lustenberger et al., 2011

Lustenberger et al., (2011) (QS:AQ(+)) completed a systematic review on the effectiveness of management approaches for trochanteric bursitis, which included non-operative approaches such as steroid injections. They identified 9 studies which studied steroids as the primary intervention including 7 x case series (Raman et al., 1982, Shbeeb et al., 1996, Rasmussen and Fano 1985, Schapira et al., 1986, Karpinski and Piggott 1985, Farmer et al., 2010, Iorio et al., 2006), 2 x RCT (Cohen et al., 2009, Rompe et al., 2009) and 1 x prospective cohort study (Sayegh et al., 2004).

There was significant heterogeneity across the studies with the mean duration of symptoms before treatment across the studies ranging from 7.1 weeks to 4.4 years. Most patients received only a single injection, but studies included patients receiving up to 5 steroid injections. All studies used a mixture of steroid and local anesthetic except Rasmussen and Fano (1988) who used methylprednisolone or triamcinolone only.

Cohen et al., (2009) compared fluoroscopically guided injection with the traditional bedside injection and found no difference in pain scores over 3 months. Subjective improvement and achieving a return to the patient’s baseline activity level ranged from 49% to 100%.

The authors concluded that for most patients, a single steroid injection provided a tangible improvement in symptoms and decrease in pain from a moderate to a low level for up to 3 years.



Abbreviations: SMD - standardised mean difference, IASI - intra-articular steroid injection

Study	QS	Conclusions	Level of Evidence
Lustenberger et al., (2011)	AQ(+)	Steroid injections resulted in reduced VAS scores in case of trochanteric bursitis	1-

		No differences between fluoroscopically guided steroid injections and the traditional bedside injection	1-
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DelBuono et al., 2012

DelBuono et al., (2012) (QS:AQ(+)) completed a systematic review into the management of GTPS, which included the use of steroid injections. They included studies of all study designs, which reported clinical, functional and imaging outcomes of patients managed for GTPS.

The identified 14 studies which met the inclusion criteria of which 5 involved steroid injections (Shbeeb et al., 1996, Rompe et al., 2009, Rasmussen and Fano 1985, Furia et al., 2009, Cohen et al., 2009). Rasmussen and Fano (1985) evaluated 36 patients after steroid injections for trochanteric bursitis. All patients reported improvement after one or two injections and 24 had excellent results. Nine patients relapsed within 2 years.

Shbeeb et al., (1996) assessed the effects on pain and functional limitation of a single local steroid injection for GTPS. Of the 75 selected patients, 20, 32 and 22 patients each received 6, 12 and 24 mg of betamethasone, respectively, mixed with 4 ml of 1% lidocaine. 77.1, 68.8 and 61.3% of responding patients reported improvement in pain at weeks 1, 6 and 26, respectively, demonstrating increased pain relief in patients receiving higher doses of betamethasone (P =0.0123).

In a double-blind RCT, Cohen et al., (2009) assessed outcomes of two groups of patients who received steroid injections with and without fluoroscopic guidance. Outcomes included pain at rest and with activity, Oswestry disability scores, SF-36 scores, reduction in drug use and patients' satisfaction at 1 and 3 months. Three months after the injection, 15 (47%) patients in the blind group and 13 (41%) in the fluoroscopy group continued to have a positive outcome, with no significant difference between the two groups.

Furia et al.,'s (2009) case-control study compared outcomes of two groups of patients with chronic GT pain syndrome. Thirty-three patients of the study group received low-energy SWT group (2000 shocks; 4 bars of pressure, equal to 0.18 mJ/mm²; total energy flux density, 360 mJ/mm²) and 33 patients received steroid injections. At 1, 3 and 12 months follow-up, Harris Hip Scores, Roles and Maudsley Score and VAS values were significantly improved from the baseline status in both groups. At 12 months there was statistically significant improvement in patients undergoing SWT than steroid injections (P < 0.001). At final follow-up, the number of patients with excellent and good results were significantly higher after SWT (P, 0.001).

Rompe et al.,(2009) allocated 229 patients to three groups including home training (progressive slow repetitive exercise including piriformis stretch, iliotibial band (ITB) stretch standing, straight leg raise, wall squat with ball and gluteal strengthening), steroid injection and SWT. Outcome measures included pain and return to pre-injury sport activity. At 1 month, steroid injection (success rate, 75%; pain rating, 2.2 points) results were significantly better than those after home training (7%; 5.9 points) or SWT (13%; 5.6 points). At 4 months, radial SWT led to significantly better results (68%; 3.1 points) than home training (41%; 5.2 points) and steroid injection (51%; 4.5 points). Fifteen months from baseline, radial SWT (74%; 2.4 points) and home training (80%; 2.7 points) were significantly more successful than was steroid injection (48%; 5.3 points). At 15 months, the home training and SWT groups were significantly

improved compared to the steroid injection group. At 4 months from baseline, 26 of 76 subjects (34%) of the home training group, 37 of 75 subjects (49%) of the corticosteroid injection group, and 50 of 78 subjects of the SWT group (64%) had been able to return to their previous levels of sports/recreational activity, with significantly higher return to sport after SWT.

Study	QS	Conclusions	Level of Evidence
DelBuono et al., (2012)	AQ(+)	In the management of GTPS, the marked short-term benefits of corticosteroid injection are reversed after a few months, with high rates of recurrence.	1-

Barratt et al., 2016

Barratt et al., (2016) (QS:AQ(+)) completed a systematic review into the management of GTPS, which included the use of steroid injections. They included all RCTs, case-control or cohort studies reporting outcome data for conservative treatments for adults having a diagnosis of GTPS, or trochanteric bursitis.

The identified 8 studies of which 5 investigated the use of steroid injections (Cohen et al., 2009, McEvoy et al., 2013, Brinks et al., 2011, Rompe et al., 2009, Shbeeb et al., 1996).

The authors concluded that based on pain, steroid injections demonstrated superior outcomes for up to 3 months compared with home training, radial shockwave therapy (RSWT) and usual care, in 4 studies demonstrating either a low or moderate risk of bias. Fluoroscopy-guided injections failed to show additional benefit.

Study	QS	Conclusions	Level of Evidence
Barratt et al., (2016)	AQ(+)	Steroid injections demonstrated superior outcomes for up to 3 months compared with home training, radial shockwave therapy (RSWT) and usual care	1-

Randomised controlled trials

Hip OA

Only one RCT not reported in the previously reported systematic reviews was found that examined the effect of intra-articular steroid injections (Lee et al., 2016). This study focused on patients with femoroacetabular impingement (FAI) syndrome. Whilst not technically osteoarthritis FAI has been identified as a mechanism for the development of early osteoarthritis for most nondysplastic hips (Ganz et al., 2003).

In this study 30 patients with clinical and radiologic evidence of FAI were randomly allocated to either a steroid injection or an intra-articular injection of hyaluronic acid at with cross-over injection at 2-weeks in patients without clinical response of decrease of pain intensity less than 2-point. Patients were followed up to 12-weeks for pain intensity, hip disability score (HOOS), oral medication and adverse events.

The authors concluded that intra-articular hip injection was effective in FAI, with faster effect of pain improvement from steroid injections and more delayed effect of function improvement by HA.

Study	QS	Conclusions
Lee et al., (2016)	AQ(+)	Intra-articular hip injection was effective in FAI, with faster effect of pain improvement from steroid injections and more delayed effect of function improvement by HA.

Greater Trochanter pain syndrome

Ribeiro et al., (2016) undertook a RCT comparing steroid injections with platelet rich plasma (PRP) injections in patients with GTPS. Eighteen patients (20 hips) with GTPS were randomized in two groups and treated with platelet rich plasma or steroid (triamcinolone) injection guided by ultrasound. Pain and function (Western Ontario McMaster and Harris Hip Score questionnaires) were evaluated prior to the intervention and after 10, 30 and 60 days. The steroid group showed pain reduction ($p=0.004$) and improved function ($p=0.036$) through the Harris Hip Score questionnaire at 10, 30 and 60 days after treatment, when compared with baseline.

The PRP group showed no statistical improvement in any of the variables.

Study	QS	Conclusions
Ribeiro et al., (2016)	AQ(+)	Intra-articular hip injection with steroid was more effective in terms of pain relief and improvement in function than PRP injections in patients with GTPS

**3.4
Outcome Measures
Pain and Function –
Recommendations**

The evidence indicates that intra-articular steroid injection to the hip joint is effective in reducing pain and improving function in the short term (<8 weeks) in patients with hip osteoarthritis. They were not effective in reducing pain and improving function in the longer term (>8 weeks) *Level A recommendation based on 1 x HQ SR (McCabe et al., 2016) and 3 x LQ SRs (Kruse 2008, Peterson and Holder 2010, Hirsch et al., 2013)*

The evidence indicates that the effectiveness of intra-articular steroid injection to the hip joint was not related to radiographic grade of osteoarthritis and clinical or sonographic evidence of inflammation or synovial hypertrophy. *Level B recommendation based on 1 x LQ SR (Hirsch et al., 2013)*

The evidence indicates that the effectiveness of intra-articular steroid injection to the hip joint was not related to the type of image guidance used. *Level B recommendation based on 1 x LQ SR (Hirsch et al., 2013)*

The evidence indicates that the effectiveness of intra-articular steroid injection to the hip joint was greater for 80 mg MPL than MPL 40mg but did not appear to be related to the volume of injectate type of image guidance used. *Level B recommendation based on 1 x LQ SR (Chandrasekaran et al., 2015)*

The evidence indicates that steroid injection to the hip is effective in reducing pain and improving function in the short term (up to 12 weeks) in patients with Greater Trochanter pain syndrome. They were not effective in reducing pain and improving function in the longer term (> 12 weeks). *Level A recommendation based on 2 x AQ SR (Barratt et al., 2016, DelBuono et al., 2012)*

The evidence indicates that fluoroscopically guided steroid injections were no more effective than traditional bedside injection in reducing hip pain in patients with Greater Trochanter pain syndrome. *Level B recommendation based on 1 x AQ SR (Lustenberger et al., 2011)*

**3.5
Outcome Measures
– Safety and Risk**

Hip OA

Kruse (2008) in their systematic review included a question related to the safety associated with intra-articular steroid injections for hip OA. The identified general risks associated with intra-articular injections anywhere in the body, including local effects such as pain with injection, post-injection flare, skin pigment changes, fat atrophy, and joint infection, and systemic changes such as disruption of diabetes and hypertension control, facial flushing, inhibition of the hypothalamo–pituitary–adrenal axis, sepsis, and death.

Specifically, for the hip, they identified three side effects of particular concern specifically related to the hip injections. These include: septic arthritis, osteonecrosis, and the risk of joint infection after total hip replacement following pre-operative intra-articular steroid injection.

The incidence of septic arthritis in the hip has not been as thoroughly studied as it has for the knee. Kruse identified 2 case reports of septic hip arthritis following steroid injection. Nallamshetty et al., (2003) reported a case of hip septic arthritis in a 65-year-old woman after intra-articular injection of betamethasone and lidocaine mixture via fluoroscopic guidance for hip pain secondary to osteoarthritis. Hip aspirate was positive for alpha-hemolytic Streptococcus. The patient required subsequent resection arthroplasty of the hip 2 months

after presentation secondary to the joint destruction. Chazerain et al., (1999) showed septic hip arthritis in a 51-year-old man following 10 intra-articular injections of sodium hyaluronate and one injection of triamcinolone between April 1995 and October 1998. The patient presented with septic arthritis in October 1998 after the last sodium hyaluronate injection. The infection was likely secondary to the increased exposure from performance of multiple repeat injections and not likely specific to the steroid therapy.

Yamamoto et al., (2006) presented the case of a 50-year-old female patient who received a single injection of methylprednisolone and sensorcaine into the hip joint, in which rapid collapse of the femoral head was noted within a 3-month period of time. Osteonecrosis of the femoral head was found on subsequent histologic analysis. General consensus proposes that osteonecrosis after joint injection is more likely related to the severity of the underlying disease and represents a natural progression of that disease rather than a side effect of the injection itself.

A paper submitted by Kaspar and de V de Beer, (2005), found in a retrospective cohort study of 80 patients a significant increase in arthroplasty revision secondary to infection in patients who had intraarticular steroid injection prior to hip replacement. The mean time between injection and surgery was 11 months, with an incidence of 10% in those who received injection compared to 0% in those who did not. The authors proposed that intraarticular injection of steroid should be considered as relatively contraindicated in patients who are candidates for hip replacement.

Two subsequent retrospective studies exploring the relationship between injection and postoperative infection do not show results consistent with the findings of the Kaspar and de V de Beer study. McIntosh et al., (2006) found in a cohort study of 437 patients, with a mean time of 112 days between injection and surgery, no significant relationship between injection and post-operative rates of infection. However, in the patients who had injection and subsequent infection, the mean time between interventions was 44 days. This was not statistically significant. The authors caution giving injections less than 2 months prior to hip replacement surgery. Chitre et al., (2007) found in 36 patients, with a mean time between injection and surgery of 18 months, no cases of deep joint sepsis during a mean follow-up time of 25.8 months.

Habib et al., (2010) in their systematic review included a review of the local risks associated with intra-articular steroid injections (including the hip).

Infections: The risk of joint infection following steroid injections is considered very low with a rate of ~1:1,000 to ~1:25,000, with a higher risk among immune compromised and incapacitated patients. However, under simple rules of antiseptic measures, the procedure is considered very safe. Relative to the frequency of injection, the hip appears to be the most infectable joint in the body. The time interval for developing clinical signs ranged from 6 days to a few weeks. A wide range of organisms had been identified as causes of infection including gram-positive and gram-negative aerobic bacteria (*Staphylococcus*, *Streptococcus* alpha, *Pseudomonas*, *Escherichia coli*), anaerobic bacteria (*Bacteroides*, *Clostridium*, *Propionibacter*), fungal (*Candida* species, *Aspergillus fumigatus*), and mycobacterium (*Mycobacterium abscessus* and *Mycobacterium avium*).

Calcifications: A common local adverse effect of steroid injection, where nearly one of 24 joints following steroid injections will end with calcifications (Gilsanz and Bernstein 1984). These calcifications are mostly pericapsular or intracapsular and rarely intraarticular, and are noted 2 months to 1 year or more following steroid injection, with the knee being the most common joint.

Charcot's arthropathy: Characterized by rapid resorption and regeneration or fragmentation of the joint that usually follows repeated steroid injections. Most joints that were reported include knees, hips, and shoulders.

Avascular necrosis: Most common joints involved are the hips (proximal femur), knees (distal femur or proximal tibial plateau), and shoulders (proximal humerus).

Rapid destruction of the femoral head: This term is used to describe a situation of joint destruction and disappearance of joint space following just one steroid injection (Yamamoto et al., 2006 (*case study*)). It is usually seen in women with unilateral hip involvement 3–12 months following the injection. Microscopically, there is total necrosis of the underlying trabecular bone and marrow tissue underneath the cartilage.

Chandrasekaran et al., (2015) in their systematic review of the evidence for the use of intra-articular steroid for the hip identified a range of local risks. These local risks included skin dislocation, fatty atrophy, exacerbation of pain, septic arthritis and a potential increased risk in infection risk of any subsequent arthroplasty procedure (Neustadt 1997 (*expert opinion*), Neidel et al., 2002 (*prospective cohort study*), Villoutreix et al., 2006 (*retrospective cohort study*), Yamamoto et al., 2006 (*case study*)).

There have been a number of case reports of septic arthritis following intra-articular steroid injections, which have mainly involved skin organisms (Apyan and Rudd 2012, Million et al., 2008, Smyth and Leidholt 1973).

McCabe et al., (2016) in their high quality systematic review identified four (4) trials that reported safety data (Lambert et al., 2007, Atchia et al., 2011, Qvistgaard et al., 2006, Kullenberg et al., 2004). Only one serious adverse event, a deep venous thrombosis 3 months post-injection, was reported in the steroid injection group (Lambert et al., 2007). The injection procedure itself was noted to be well tolerated in all studies. No adverse events in the steroid injection groups were reported in two trials (Lambert et al., 2007, Qvistgaard et al., 2006)

One trial found similar rates of adverse events (52% placebo group vs 51% in the steroid group), and noted that 'most were mild and/or considered unrelated to treatment (Lambert et al., 2007). Qvistgaard et al., (2006) noted that three patients (out of a total sample of 101) experienced a flare in pain post-injection but did not allocate these to a specific treatment group.

Greater Trochanter pain syndrome

Del Buono et al., (2012) in their systematic review of management of GTPS reported that in one study (Rompe et al., 2009) comparing steroid injection with SWT that 9 of 75 patients in the steroid group (12%) and 29 of 78 (37.2%) patients in shock wave group complained of skin irritation and swelling.

Recommendations

Minor complications associated with intra-articular steroid injections into the hip are not uncommon but rarely require significant medical attention. Whilst serious complications are rare, the hip joint appears susceptible to conditions such as calcifications and necrosis of the femoral head. Increased risk appears related to technique and repeated injections.

Level A recommendation

Minor complications associated with steroid injections into the hip for Greater Trochanter pain syndrome are not uncommon but rarely require significant medical attention. *Level B recommendation*

**3.6
Economic analysis**

This review found no evidence related to the economic analysis of intra-articular steroid injections for hip osteoarthritis or of steroid injections for Greater Trochanter Pain Syndrome.

DRAFT

4. Recommendations

Summary of Recommendations

The evidence indicates that intra-articular steroid injection to the hip joint is effective in reducing pain and improving function in the short term (<8 weeks) in patients with hip osteoarthritis. They were not effective in reducing pain and improving function in the longer term (>8 weeks) *Level A recommendation based on 1 x HQ SR (McCabe et al., 2016) and 3 x LQ SRs (Kruse 2008, Peterson and Holder 2010, Hirsch et al., 2013)*

The evidence indicates that the effectiveness of intra-articular steroid injection to the hip joint was not related to radiographic grade of osteoarthritis and clinical or sonographic evidence of inflammation or synovial hypertrophy *Level B recommendation based on 1 x LQ SR (Hirsch et al., 2013)*

The evidence indicates that the effectiveness of intra-articular steroid injection to the hip joint was not related to the type of image guidance used. *Level B recommendation based on 1 x LQ SR (Hirsch et al., 2013)*

The evidence indicates that the effectiveness of intra-articular steroid injection to the hip joint was greater for 80 mg MPL than MPL 40mg but did not appear to be related to the volume of injectate type of image guidance used. *Level B recommendation based on 1 x LQ SR (Chandrasekaran et al., 2015)*

The evidence indicates that steroid injection to the hip is effective in reducing pain and improving function in the short term (up to 12 weeks) in patients with Greater Trochanter pain syndrome. They were not effective in reducing pain and improving function in the longer term (> 12 weeks) *Level A recommendation based on 2 x AQ SR (Barratt et al., 2016, DelBuono et al., 2012)*

The evidence indicates that fluoroscopically guided steroid injections to the hip were no more effective than traditional bedside injection in reducing pain in patients with Greater Trochanter pain syndrome. *Level B recommendation based on 1 x AQ SR (Lustenberger et al., 2011)*

Minor complications associated with intra-articular steroid injections into the hip are not uncommon but rarely require significant medical attention. Whilst serious complications are rare, the hip joint appears susceptible to conditions such as calcifications and necrosis of the femoral head. Increased risk appears related to technique and repeated injections. *Level A recommendation*

Minor complications associated with steroid injections into the hip for Greater Trochanter pain syndrome are not uncommon but rarely require significant medical attention. *Level B recommendation*

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6. Appendices

Appendix 1: Sign Checklists Used in this Review SIGN Critical Appraisal Tool for Systematic Reviews and Meta-analyses


 SIGN	Methodology Checklist 1: Systematic Reviews and Meta-analyses SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: <i>Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C., et al.,... Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from http://www.biomedcentral.com/1471-2288/7/10 [cited 10 Sep 2012]</i>	
Study identification (Include author, title, year of publication, journal title, pages)		
Guideline topic:		Key Question No:
Before completing this checklist, consider: Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.		
Checklist completed by:		
Section 1: Internal validity		
In a well conducted systematic review:		Does this study do it?
1.1	The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	Yes <input type="checkbox"/> No <input type="checkbox"/> If no reject
1.2	A comprehensive literature search is carried out.	Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable <input type="checkbox"/> If no reject
1.3	At least two people should have selected studies.	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.4	At least two people should have extracted data.	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.5	The status of publication was not used as an inclusion criterion.	Yes <input type="checkbox"/> No <input type="checkbox"/>
1.6	The excluded studies are listed.	Yes <input type="checkbox"/> No <input type="checkbox"/>
1.7	The relevant characteristics of the included studies are provided.	Yes <input type="checkbox"/> No <input type="checkbox"/>
1.8	The scientific quality of the included studies was assessed and reported.	Yes <input type="checkbox"/> No <input type="checkbox"/>
1.9	Was the scientific quality of the included studies used appropriately?	Yes <input type="checkbox"/> No <input type="checkbox"/>
1.10	Appropriate methods are used to combine the individual study findings.	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/> Not applicable <input type="checkbox"/>
1.11	The likelihood of publication bias was assessed appropriately.	Yes <input type="checkbox"/> No <input type="checkbox"/>

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		Not applicable <input type="checkbox"/>
1.12	Conflicts of interest are declared.	Yes <input type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review?	High quality (++) <input type="checkbox"/> Acceptable (+) <input type="checkbox"/> Low quality (-) <input type="checkbox"/> Unacceptable – reject 0 <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes:	

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SIGN Critical Appraisal Tool for Controlled trials

 SIGN	<h2>Methodology Checklist 2: Controlled Trials</h2>	
Study identification (<i>Include author, title, year of publication, journal title, pages</i>)		
Guideline topic:	Key Question No:	Reviewer:
<p>Before completing this checklist, consider:</p> <ol style="list-style-type: none"> 1. Is the paper a randomised controlled trial or a controlled clinical trial? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a controlled clinical trial questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+ 2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist. 		
Reason for rejection: 1. Paper not relevant to key question <input type="checkbox"/> 2. Other reason <input type="checkbox"/> (please specify):		
SECTION 1: INTERNAL VALIDITY		
<i>In a well conducted RCT study...</i>		<i>Does this study do it?</i>
1.1	The study addresses an appropriate and clearly focused question.	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.2	The assignment of subjects to treatment groups is randomised.	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.3	An adequate concealment method is used.	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.4	The design keeps subjects and investigators 'blind' about treatment allocation.	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.5	The treatment and control groups are similar at the start of the trial.	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.6	The only difference between groups is the treatment under investigation.	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/> Does not apply <input type="checkbox"/>
1.10	Where the study is carried out at more than one site, results are comparable for all sites.	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/> Does not apply <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		

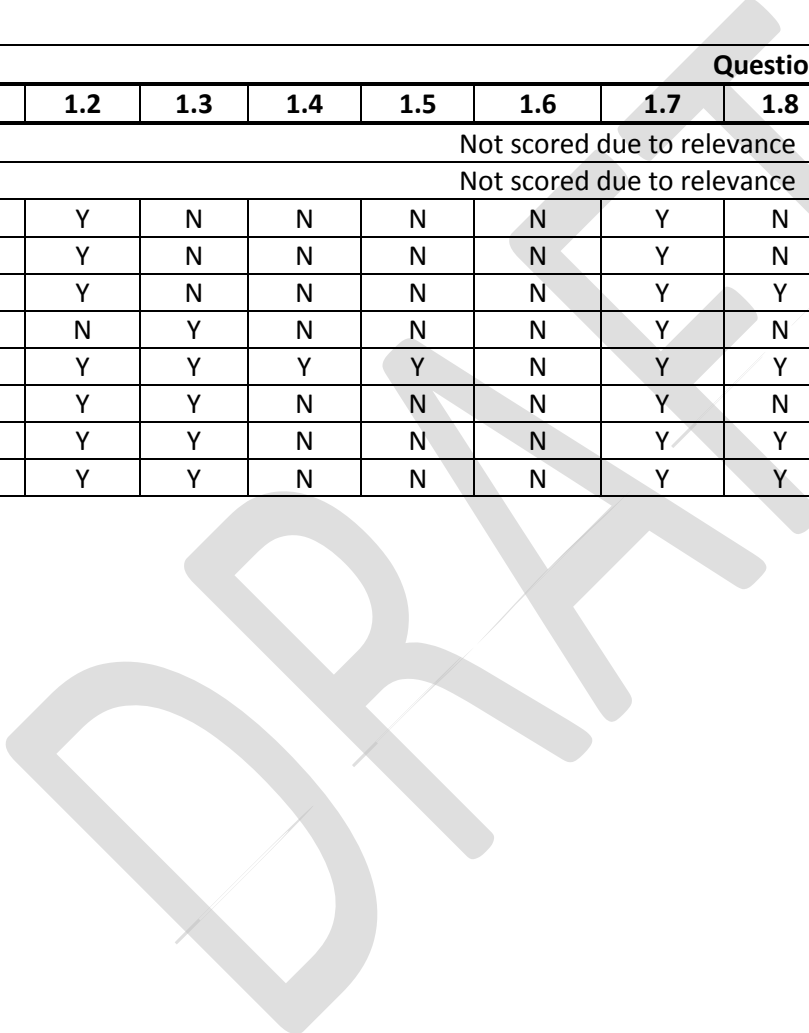
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2.1	How well was the study done to minimise bias? <i>Code as follows:</i>	High quality (++) <input type="checkbox"/> Acceptable (+) <input type="checkbox"/> Low quality (-) <input type="checkbox"/> Unacceptable – reject 0 <input type="checkbox"/>
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	
2.4	Notes. Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.	

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Appendix 2: Quality scores for systematic reviews used in this review

Reference (author, year)		Question													
Study	Year	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.8	1.9	1.10	1.11	1.12	2.1	2.2
Zhang et al.,	2007	Not scored due to relevance												RQ(-)	N
Zhang et al.,	2010	Not scored due to relevance												RQ(-)	N
Kruse et al.,	2008	Y	Y	N	N	N	N	Y	N	N	Y	N	N	LQ(-)	Y
Peterson and Hodler	2010	N	Y	N	N	N	N	Y	N	N	Y	N	N	LQ(-)	Y
Hirsch et al.,	2013	Y	Y	N	N	N	N	Y	Y	N	Y	N	n	LQ(-)	Y
Chandrasekaran et al.,	2015	Y	N	Y	N	N	N	Y	N	N	Y	N	N	LQ(-)	Y
McCabe et al.,	2016	Y	Y	Y	Y	Y	N	Y	Y	N	Y	N	Y	HQ(++)	Y
Lustenberger et al.,	2011	Y	Y	Y	N	N	N	Y	N	N	Y	N	Y	AQ (+)	Y
DelBuono et al.,	2012	Y	Y	Y	N	N	N	Y	Y	N	Y	N	Y	AQ (+)	Y
Barratt et al.,	2016	Y	Y	Y	N	N	N	Y	Y	N	Y	N	Y	AQ (+)	Y



Appendix 3: Data extraction for systematic reviews included in this review

Author and year	SIGN Score	Studies (patient No)	Outcome	Conclusions	Evidence				Grade
					1	2	3	4	
HIP OA									
Zhang et al., (2007/10)	RQ(-)	23 guidelines	Pain, Function	Failed to differentiate between hip and knee OA so the findings are not relevant to this review	0	0	0	1	1-
Kruse (2008)	LQ(-)	8 Studies 4 RCTs; (n=268)	Pain, Function	Short term reduction (up to 12 weeks) in pain and function with intra-articular steroid injection for OA of the hip	0	0	0	1	1-
Peterson and Holder (2010)	LQ(-)	3 RCTs (n=233)	Pain, function	Steroid injections provide short-term improvement in pain and function (2–3 months) in patients with hip OA, particularly for night pain, but that they are not effective for long-term pain relief.	0	0	0	0	1-
Hirsch et al., (2013)	LQ(-)	8 Studies 5 RCTs; (n=586)	Pain, function	No factors appear as potential predictor of response to steroid injection to the hip, including radiographic grade and clinical or sonographic evidence of inflammation or synovial hypertrophy	0	0	1	0	1-
Chandrasekaran et al., (2015)	LQ(-)	26 studies 3 RCTs, 10 Prospective trial, 13 retrospective studies (n=NS)	Pain, function	Intra-articular steroid injection for hip OA was a significant reduction in pain and improvement in hip scores for up to 12 weeks,	0	0	0	0	1-
				80 mg MPL produces a sustained improvement in pain, stiffness and function compared with 40 mg MPL	0	0	0	0	1-
				The volume of injection alone did not affect efficacy.	0	0	0	0	1-
McCabe et al., (2016)	HQ(++)	5 RCTs (n=345)	Pain, Function	Intra-articular steroid injection for hip OA was a significant reduction in pain and improvement in hip scores in the short term (up to 8 weeks)	1	1	1	0	1+
GTPS									
Lustenberger et al., (2011)	AQ(+)	12 studies 3 RCTs, 7 case series, 1 prospective cohort study; (n= 950)	Pain, function	Steroid injections resulted in reduced VAS scores in case of trochanteric bursitis	0	1	0	0	1-
				No differences between fluoroscopically guided steroid injections and the traditional bedside injection	0	1	0	0	1-
DelBuono et al., (2012)	AQ(+)	14 studies 2 RCTs 1 Prospective cohort, 11 case studies	Pain, Function	In the management of GTPS, the marked short-term benefits of corticosteroid injection are reversed after a few months, with high rates of recurrence.	0	1	0	0	1-
Barratt et al., (2016)	AQ(+)	8 studies, 3 RCTs, 2 prospective cohorts and 2 retrospective cohort (n=696)	Pain, Function	Steroid injections demonstrated superior outcomes for up to 3 months compared with home training, radial shockwave therapy (RSWT) and usual care	0	1	0	0	1-

Appendix 4: RCTs within the systematic reviews used in this study

	Kruse et al., 2008	Peterson and Holder (2010)	Hirsch et al., (2013)	Chandrasekaran et al., (2015)	McCabe et al., (2016)	Lustenberger et al., (2011)	DelBuono et al., (2012)	Barratt et al., (2016)
Hip OA								
Lambert et al., 2007,	1	1	1		1			
Flanagan et al., 1988	1		1		1			
Qvistgaard et al., 2006,	1	1	1		1			
Kullenberg et al., 2004,	1	1		1	1			
Young et al., 2012			1	1				
Atchia et al., 2011			1		1			
Deshmukh et al., 2011,			1					
Plant et al., 1997,			1					
Robinson et al., 2007			1	1				
GTPS								
Cohen et al., 2009,						1	1	1
Rompe et al., 2009						1	1	1
Brinks et al., 2011								1
	4	3	8	3	5	2	2	3

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Appendix 5: Quality scores for randomised controlled trials used in this review

Reference (author, year)		Questions												
Study	Year	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.8	1.9	1.10	2.1	2.2	2.3
Lee et al.,	2016	Y	Y	Y	Y	CS	Y	Y	60%	N	NA	AQ(+)	Y	Y
2.4	Intra-articular hip injection may be effective in FAI, with faster effect of pain improvement by TA and more delayed effect of function improvement by HA.													
Ribeiro et al.,	2016	Y	Y	Y	Y	CS	Y	Y	CS	N	NA	AQ(+)	Y	Y
2.4	Up to 60 days, PRP infiltration has no influence on pain relief and function improvement in trochanteric syndrome treatment.													

Systematic Review:
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Appendix 6: Data extraction for randomised controlled trials used in this review

Study	Subjects			Intervention	Comparator	Outcome measures	Time	Results
	N=	Age	Diagnosis					
Behera et al. (2015)	25	27-50	Lateral epicondylar tendinopathy of the humerus > 3/12	Bupivacaine 3ml	Leukocyte-poor platelet-rich plasma	Pain (VAS; Nirschl score) MMCPiE (function and movement)	Baseline, 1 Month, 3 months, 6 months, 1 year	<ul style="list-style-type: none"> After one month, improvement was less in the PRP than bupivacaine group in terms of the VAS for pain (17.7% vs. 26.5%), MMCPiE score (24.0% vs. 27.6%), and Nirschl score (20.7% vs. 31.1%). Improvement was greater in the PRP than bupivacaine group after 3 months (42.5% vs. 30.9%, 34.1% vs. 27.2%, and 50.7% vs. 39.6%), 6 months (67.3% vs. 20.1%, 40.6% vs. 16.3%, and 71.4% vs. 31.1%), and one year (83.2% vs. 45.6%, 47.0% vs. 21.7%, and 76.6% vs. 56.3%). The differences in scores between groups were significant at 6 months and one year only (p<0.001).
Bellapianta et al. (2011)	19	NR	Acute symptomatic lateral epicondylitis (<6 months);	Triamcinolone (10mg) + Lidocaine	Peppering vs single injection	Pain (VAS), Grip Strength, DASH	Baseline and 10 wks	Single injections performed better than peppering
Beyazal & Devrimsel (2015)	64	26-57	Lateral epicondylitis	Methylprednisolone acetate (20mg) + prilocaine	ESWT	Pain (VAS, McGill pain Q), Grip strength	Baseline, 4 & 12 wks	<ul style="list-style-type: none"> ESWT better results across all outcome measures than steroid injections
Carayannopoulos et al. (2011)	24	18-75	Lateral epicondylitis (3/12 to 2 years)	Methylprednisolone acetate 40mg + procaine	Prolotherapy	Pain (VAS), Grip Strength, DASH	Baseline, 1, 3, 6 mths;	<ul style="list-style-type: none"> No significant differences between the prolotherapy and the corticosteroid group for change in VAS, QVAS, or DASH. Both improved from baseline
Gunduz (2012)	59	43-46	Pain lateral elbow < 3 months	Methylprednisolone acetate 20mg + procaine	Physiotherapy and ESWT	Pain (VAS), Grip Strength,	Baseline, 1, 3, 6 mths	<ul style="list-style-type: none"> All treatment improved similarly
Küçükşen et al. (2013)	82	18-72	Pain lateral elbow > 3 months	Triamcinolone 40mg + lidocaine	Muscle energy technique	Pain (VAS), Grip Strength, DASH	Baseline, 6, 26, 52 wks	<ul style="list-style-type: none"> Both MET and CSI improved measures of strength, pain, and function compared to baseline, however CSI was more effective in the short term (>6wks) while MET scored more highly for the long term (<52wks)



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Study	Subjects			Intervention	Comparator	Outcome measures	Time	Results
	N=	Age	Diagnosis					
Lebiedzinski et al. (2015)	120	21-96	Acute symptomatic lateral epicondylitis (<6 weeks);	Betamethasone 10mg + lidocaine	autologous conditioned plasma	Pain, DASH	baseline, 6wks, 6 & 12 mths	<ul style="list-style-type: none"> • ACP better at 12 months; CSI has more rapid improvement. Therapeutic effect is longer lasting in ACP group.
Murtezani et al. (2015)	60	>18yrs	Lateral epicondylitis (<3/12)	Triamcinolone acetonide 10mg + lidocaine	Exercise and Ultrasound	Pain (VAS) PRTEE score, Grip strength	Baseline, 6wk, 12 wk	<ul style="list-style-type: none"> • Exercise group sig. improvements across all outcome measures compared to CSI @ 12wks
Stefanou et al. (2012)	101	18-71	Lateral epicondylitis (> 2 years)	Dexamethasone or triamcinolone 10mg	Dexamethasone (10mg) via iontophoresis	PRTEE score, Grip strength, work status	Baseline, 8 weeks, 6 months	<ul style="list-style-type: none"> • By 6-month all groups had equivalent significant results for all measured outcomes. • The iontophoresis patients had statistically significant improvement in grip strength at 8 weeks. They were also more likely to get back to work without restriction at 8 weeks.
Tahririan et al. (2014)	78	32-65	Acute symptomatic lateral epicondylitis (<6 weeks);	Depomedrol (40mg)	control +/- splinting	Pain (VAS), Oxford Elbow Scal	Baseline, 2, 4, & 24 wks	<ul style="list-style-type: none"> • CSI sig. pain reduction in short term, • No benefit in comparison to control by 24th week
Weerakul & Galassi (2012)	112	46	Lateral epicondylitis	High dose Triamcinolone 10mg + lidocaine	Low dose Triamcinolone 5mg + lidocaine	Pain (VAS) grip strength	Baseline & 12 wks	<ul style="list-style-type: none"> • <i>There were no statistically significant in terms of patient satisfaction, pain score, tenderness at lateral epicondyle, grip strength and adverse effect rate</i>
Yadav (2015)	65	21-60	Lateral epicondylitis (<6/12)	Methylprednisolone 40mg	Platelet-rich plasma	Pain (VAS), Grip Strength, DASH	Baseline, 15 days, 1 & 3 mths	<ul style="list-style-type: none"> • PRP and CSI both are effective in the treatment of lateral epicondylitis. However, PRP is a superior treatment option for longer duration efficacy.
Ahmed et al. (2012)	60	>18	Lateral epicondylitis (<3/12)	Triamcinolone 20mg + Lidocaine	Topical and oral NSAID	Pain (VAS)	Baseline 6/52, 12/52	<ul style="list-style-type: none"> • In patients with LE, the use of local steroid injection in combination with topical and oral NSAIDs is superior to the use of combination of topical and oral NSAIDs. Better results with combination therapy using local steroid injection may be limited to the short term.

Systematic Review:
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Study	Subjects			Intervention	Comparator	Outcome measures	Time	Results
	N=	Age	Diagnosis					
Guo et al. (2016)	26	Ave 51yrs	Lateral epicondylitis (>6/12)	Triamcinolone acetate 40mg	Botox	Pain (VAS), Grip Strength, PRTEE	Baseline, 4, 8, 12, and 16 weeks	<ul style="list-style-type: none"> At 4 weeks Steroids were superior to the Botox injection at the tender point in improvement on the visual analogue scale (p=0.006), grip strength (p=0.03) and Patient-Rated Tennis Elbow Evaluation (p=0.02). However, these differences were not observed at the 8-, 12-, and 16-week follow-ups. There was no significant difference between the Steroid and Botox to the enthesis groups.
Palacio et al. (2016)	60	22-85	Lateral epicondylitis	Dexamethasone 3ml	platelet-rich plasma (PRP)	DASH, PRTEE	Baseline, 3 months, 6 months	<ul style="list-style-type: none"> At a significance level of 5%, there was no evidence that one treatment was more effective than another, when assessed using the DASH and PRTEE questionnaires.
Khaliq et al. (2015)	102		Lateral epicondylitis	methylprednisolone acetate 2ml + xylocaine 1ml	platelet-rich plasma (PRP)	Pain (VAS)	Baseline, 3 weeks	<ul style="list-style-type: none"> PRP more effective in reducing pain at 3 weeks than steroid injection.
Bahari et al. (2003)	38	mean 42.55 & 42.7	Medial epicondylitis	Methylprednisolone, 40mg + 1ml Lidocaine	Saline + 1ml Lidocaine	Nirschl and Pettrone grading 0 - 4 severity of pain	Baseline, 2, 4, & 12 months	<ul style="list-style-type: none"> The severity of pain in both groups was same before the treatment and there was no significant difference between the two groups. The difference in pain score between the two groups at 2 months was statistically significant (p = 0.01). At 4 months, the mean pain scores in the two groups were similar (p = 0.673) and there were no significant differences between the two groups at 12 months (p = 0.942, Mann-Witney test)
Stahl & Kaufman (1997)	58	43(1.2 2) years	Medial epicondylitis	Methylprednisolone, 40mg+ 1ml Lidocaine	platelet-rich plasma (PRP)	Nirschl and Pettrone grading 0 - 4 severity of pain; VAS	Baseline, 6 week, 3 & 12 months	<ul style="list-style-type: none"> Experimental group sig. less pain than control group at 6 wks on Nirschl & Pettrone, but groups did not differ at 3 & 12 mths. No difference on VAS for any time point.