Use and Safety of Corticosteroid Injections: Joints and Musculoskeletal Soft Tissue Injections. *Guidelines from the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, the American Society of Interventional Pain Physicians, the International Pain and Spine Intervention Society, and the North American Spine Society* 

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AAPM	American Academy of Pain Medicine
ACs	Adhesive capsulitis
AEs	Adverse effects
ANA	Antinuclear antibodies
ASRA PM	American Society of Regional Anesthesia and Pain Medicine
ASIPP	American Society of Interventional Pain Physicians
BMD	Bone mineral density
BMI	Body mass index
CDC	Centers for Disease Control
CRP	C-reactive protein
<del>CS</del>	Corticosteroid
CSI	Corticosteroid injection
DASH	Disabilities of the Arm, Shoulder, and Hand
DM	Diabetes mellitus
ESHS	External snapping hip syndrome
ESR	Erythrocyte sedimentation rate
EULAR	European League Against Rheumatism
FBG	Fasting blood glucose
GTPS	Greater trochanteric pain syndrome
HIV	Human immunodeficiency virus
H	Intraarticular
HACS	Intraarticular corticosteroid injection
IPSIS	International Pain and Spine Intervention Society
ISHS	Internal Snapping Hip Syndrome
LE	Lateral epicondylitis/epicondylosis
ME	Medial epicondylitis/epicondylosis
MPA	Methylprednisolone acetate
NASS	North American Spine Society
NSAIDs	Nonsteroidal anti-inflammatory drugs
<del>0A</del>	Osteoarthritis
OARSI	Osteoarthritis Research International
PG	Practice Guideline
PH	Prosthetic joint infection
PRP	Platelet rich plasma
PT	Physical Therapy
RA	Rheumatoid arthritis
ROM	Range of motion
RPOA	Rapid progressive osteoarthritis
RCT	Randomized controlled trial
<del>SASDB</del>	Subacromial subdeltoid bursa
SHS	Snapping hip syndrome
SPADI SPADI	Shoulder Pain and Disability Index
SR	Statements and Recommendations
TA	Triamcinolone acetonide

TH	Triamcinolone hexacetonide
THR	Total hip replacement
TKR	Total knee replacement
<del>US</del>	Ultrasound
USG	Ultrasound guided
VAS	Visual Analog Scale
<b>WOMAC</b>	Western Ontario and McMaster Universities Arthritis Index

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### Abstract

**Background:** Intra-articular and peri-articular corticosteroid injections are commonly used to treat musculoskeletal conditions. Results vary by musculoskeletal region, but most studies report short-term benefit with mixed results on long-term relief. Publications showed adverse events from single corticosteroid injections. Recommended effective doses were lower than those currently used by clinicians.

Methods: Development of the practice guideline for joint injections\_was approved by the Board of Directors of the American Society of Regional Anesthesia and Pain Medicine and the participating societies. A Corticosteroid Safety Work Group coordinated the development of three guidelines: peripheral nerve blocks and trigger points; joints; and neuraxial, facet, and sacroiliac joint injections. The topics included safety of the technique in relation to landmarkguided, ultrasound or radiology aided injections; effect of the addition of the corticosteroid on the efficacy of the injectate; and adverse events related to the injection. Experts on the topics were assigned to extensively review the literature and initially develop consensus Statements and Recommendations. The United States Preventive Services Task Force grading of evidence and strength of recommendation was followed. A modified Delphi process was adhered to in arriving at a consensus.

**Results:** This guideline focuses on the safety and efficacy of corticosteroid joint injections for managing joint chronic pain in adults. The joints that were addressed included the shoulder, elbow, hand, wrist, hip, knee, and small joints of the hands and feet. All the Statements and Recommendations were approved by all participants and the Board of Directors of the participating societies after four rounds of discussion. There is little evidence to guide selection of one corticosteroid over another. Ultrasound guidance increases the accuracy of injections and

reduces procedural pain. A dose of 20 mg triamcinolone is as effective as 40 mg for both shoulder intraarticular corticosteroid and subacromial subdeltoid bursa corticosteroid injections. The commonly used dose for hip intraarticular corticosteroid injections (IACS) is 40 mg triamcinolone or methylprednisolone. Triamcinolone 40 mg is as effective as 80 mg for knee IACS. Overall, IACS injections result in short-term pain relief from a few weeks to a few months. The adverse events include increase in blood glucose, adrenal suppression, detrimental effect on cartilage lining the joint, reduction of bone mineral density, and postoperative joint infection.

**Conclusions:** In this practice guideline, we provided specific recommendations on the role of corticosteroids in joint, bursa, and peritendon injections for musculoskeletal pain.

#### Joint injections for adult chronic pain and the role of corticosteroids

Pain in the shoulder, hip, knees, or fingers, is common in patients over 40 years of age.<sup>4</sup> Degenerative joint disease is a consequence of repeated trauma, metabolic disease, or autoimmune disease.<sup>2</sup> The mechanisms for joint pain include the local release of proinflammatory cytokines, neurotransmitters, and growth factors that stimulate nociceptors, Adelta and C fibers.<sup>3</sup> Sympathetic nerves and low-threshold mechanoreceptors may be involved in generating and propagating pain signals in degenerative joint disease. The pain signal is modulated within the spinal cord and brain; central sensitization may contribute to amplification and continuation of the pain sensation.

The diagnosis and management of joint pain has been described<sup>+</sup> and is beyond the scope of this guideline. However, it is important to identify pathology and pain generators in complex joints such as the shoulder joint (acromioclavicular or glenohumeral joint, subacromial subdeltoid bursa, biceps tendon), and the hip joint (trochanteric bursa gluteus medius/minimus tendon, iliopsoas bursa) to ensure injection at the appropriate location. Peripheral joint injections are utilized after failure of conservative management with the objective of reducing pain and improving function. IACS and other musculoskeletal injections alleviate inflammation and reduce pain, improve function, facilitate rehabilitation, or give some temporary relief until definitive treatment, for example surgery, can be undertaken. Injectates include local anesthetic, hyaluronic acid, platelet rich plasma (PRP), mesenchymal stromal cells, and corticosteroid.<sup>2</sup> The data is most robust for corticosteroid injections (CSIs).

CSIs fall into three broad categories: peripheral nerve blocks; joints and bursa; and neuraxial. CSIs are common procedures for patients with joint pain, such injections are

performed using landmark techniques or aided by US or fluoroscopy. Several studies revealed corticosteroid-related adverse events; these include decrease in bone mineral density (BMD), inhibition of the hypothalamic pituitary axis, increase in blood sugar, and postoperative joint infection. These events are compounded by clinicians injecting amounts higher than minimally effective doses. Regarding safety of the different techniques, there has been no publication that compared the safety of the different procedures with landmark, US, or fluoroscopy, across the joints' spectrum.

Cognizant of the above problems, the American Society of Regional Anesthesia and Pain Medicine (ASRA PM) authorized the development of practice guidelines (PGs) that address these issues. In this PG, we discuss the rationale, mechanisms and efficacy of, and adverse events from corticosteroid injections into peripheral joints and related musculoskeletal structures (e.g., tendons, ligaments, and bursa). This is the second of three PGs that the Corticosteroid Safety Work Group developed. The first is the recently published PG on sympathetic and peripheral nerve blocks, and trigger point injections;<sup>4</sup> the third is on facet, and sacroiliac joint injections, and associated topics including vaccine and anticoagulants (in preparation); and, the fourth is on neuraxial injections.

The guidelines are not intended to limit or deny care nor affect the rights of patients or providers nor do they define standard of care. They are not intended to replace clinical judgment. In the imperfect setting of heterogenous data, limited data, controversial topics, and bias inherent to expert opinion, compliance with the recommendations may not result in improved outcomes compared with personalized medicine.

Development of the practice guideline

The Corticosteroid Safety Work Group consisted of experts who have written on the subject. The Work Group decided on the topics for the PGs and recruited additional experts to develop SRs. The project was sponsored by the American Society of Regional Anesthesia and Pain Medicine (ASRA PM), the participating societies included the American Academy of Pain Medicine (AAPM), American Society of Interventional Pain Physicians (ASIPP), North American Spine Society (NASS), and International Pain and Spine Intervention Society (IPSIS). The American College of Rheumatology (ACR), American Academy of Orthopaedic Surgeons (AAOS), and the American Academy of Physical Medicine and Rehabilitation (AAPM&R) identified members with content expertise (JF, JR and AN, respectively) who helped create the SRs, participated in the discussions, and voted on the SRs.

In this PG, the joints covered include shoulder, elbow, hip, knee, hand, wrist, and small joints. Each member of the Writing Committee was assigned a topic, extensively searched the literature using PubMed, EMBASE, and/or Cochrane clinical trials with appropriate MeSH (see **Supplemental Appendix**), and initially formulated Statements and Recommendations (SRs) using a modified United States Preventive Services Task Force (USPSTF) levels of evidence (Table 1).<sup>5</sup>

Grade	<b>Definitions</b>	Suggestions for Practice
A	The Multisociety Corticosteroid Safety Work	Offer or provide this service.
	Group recommends the service. There is high	
	certainty that the net benefit is substantial.	
₿	The Multisociety Corticosteroid Safety Work	Offer or provide this service.
	Group recommends the service. There is high	
	certainty that the net benefit is moderate, or	
	there is moderate certainty that the net	
	benefit is moderate to substantial.	
e	The Multisociety Corticosteroid Safety Work	Offer or provide this service for
	Group recommends selectively offering or	selected patients depending on
	providing this service to individual patients	individual circumstances.
	based on professional judgment and patient	
	preferences. There is at least moderate	
	certainty that the net benefit is small.	
₽	The Multisociety Corticosteroid Safety Work	Discourage the use of this service.
	Group recommends against the service.	<b>-</b>
	There is moderate or high certainty that the	
	service has no net benefit or that the harms	
	outweigh the benefits.	
Ŧ	The Multisociety Corticosteroid Safety Work	Read the clinical considerations
	Group concludes that the current evidence is	section of USPSTF Recommendation
	insufficient to assess the balance of benefits	Statement. If the service is offered,
	and harms of the service. Evidence is	patients should understand the
	lacking, of poor quality, or conflicting, and	uncertainty about the balance of
	the balance of benefits and harms cannot be	benefits and harms.
	determined.	

### Table 1. Modified United States Preventive Services Task Force (USPSTF) Grades and Suggestions for Practice

\*The USPSTF defines certainty as "likelihood that the USPSTF assessment of the net benefit of a service is correct." The net benefit is defined as benefit minus harm of the service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a service.

From: Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: a review of the process. *Am J Prev Med.* Apr 2001;20(3 S):21-35.<sup>5</sup>

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-
	designed, well conducted studies in representative care populations with
	joint pain. These studies assess the effects of the service on health outcomes
	This conclusion is therefore unlikely to be strongly affected by the results of
	future studies.
	Examples - Randomized Controlled Trials or large scale observational
	studies with control groups
Moderate	The available evidence is sufficient to determine the effects of the
	intervention on health outcomes, but confidence in the estimate is
	constrained by such factors as:
	<ul> <li>The number, size, or quality of individual studies.</li> </ul>
	<ul> <li>Inconsistency of findings across individual studies.</li> </ul>
	<ul> <li>Limited generalizability of findings to individuals with joint pain</li> </ul>
	<ul> <li>Different etiologies and phenotypes in the study subjects with joint</li> </ul>
	pain.
	<ul> <li>Lack of coherence in the chain of evidence.</li> </ul>
	As more information becomes available, the magnitude or direction of the
	observed effect could change, and this change may be large enough to alter
	the conclusion.
	Examples A single large scale observational study without control groups
	(multisite or single site); Multiple (>2) large retrospective studies (>20
	subjects) or cohort studies.
Low	The available evidence is insufficient to assess effects on health outcomes.
	Evidence is insufficient because of:
	<ul> <li>The limited number or size of studies.</li> </ul>
	<ul> <li>Important flaws in study design or methods.</li> </ul>
	<ul> <li>Inconsistency of findings across individual studies.</li> </ul>
	<ul> <li>Gaps in the chain of evidence.</li> </ul>
	<ul> <li>Findings not generalizable to individuals with joint pain, or</li> </ul>
	generalizable only to a small proportion of those with joint pain.
	<ul> <li>Lack of information on important health outcomes.</li> </ul>
	More information may allow estimation of effects on health outcomes.
	Examples: Case series or case reports or consensus based recommendations
	from other sources

Table 2. Modified United States Preventive Services Task Force (USPSTF) Levels of Certainty

The SRs were modified after several discussions involving all the participants, using a modified Delphi process<sup>6,7</sup> and unanimously approved after four rounds of voting. Subsequently, the Statements and Recommendations were approved by the Board of Directors of the participating societies.

### **Indications and composition of corticosteroid injections**

Joint pain can be debilitating and limit a patient's mobility, activity, and quality of life. Intra-articular corticosteroid (IACS) injections are employed for the management of pain related to arthropathy due to osteoarthritis (OA), rheumatoid arthritis (RA) and other inflammatory arthritis (e.g., crystalline, psoriatic, or spondyloarthropathy); hemophilic arthropathy; or posttraumatic arthritis. In addition, these injections may also be used for recalcitrant soft tissue injuries tendinosis/tendinitis, and bursitis. Conventional conservative management, including exercise, weight loss, physiotherapy, and anti-inflammatory medications, is usually undertaken for joint pain. IACS injections are usually employed when non-pharmacological treatment and analgesics fail to provide adequate relief of the symptoms. A review of more focused (usually single joint) clinical PGs noted the recommendations of higher-quality PGs: guidelines that scored at least 60% for domains 3 (rigor of development), 6 (editorial independence), plus one other criterion in the AGREE II tool.<sup>8</sup> These prior PGs consistently recommended education, exercise, and weight management, nonsteroidal anti-inflammatory drugs (NSAIDs) for hip and knee OA, and IACS for knee. Other recommendations were less consistent, these included paracetamol, IACS for hip OA, hyaluronic acid for knee OA, and acupuncture. Arthroscopy was consistently recommended against.<sup>8</sup> An update of the EULAR PG added appropriate footwear, assistive devices, modifying work-related factors, and behavioral changes to the previous recommendations.9

### Hip and knee IACS practice recommendations from organizations

Indications for IACS and other soft tissue musculoskeletal injections include pain relief and improved function. In 2019, The American College of Rheumatology (ACR) updated their 2019 recommendations for hip and knee IACS.<sup>10</sup> In patients with knee and hip OA, a strong

recommendation was made for IACS (Box 1). The American Academy of Orthopaedic Surgeons
(AAOS) updated their advice from "unable to recommend (knee)", <sup>11,12</sup> to "could be considered"
in their most recent version. <sup>13,14</sup> The European League Against Rheumatism EULAR)
recommended the injection of a long-acting GC for acute exacerbation of knee pain, especially if
accompanied by effusion. <sup>15</sup> For hip OA, they changed their original advice from "not
recommended", <sup>16</sup> to "maybe considered in patients with flare that is unresponsive to analgesic or
NSAID."17 This was prompted by an RCT that showed better results with IACS compared to
local anesthetic alone and two uncontrolled trials showed some short term (3 months) pain
reduction from IACS injection. <sup>17</sup> The Osteoarthritis Research Society (OARSI) <sup>18</sup> conditionally
recommended IACS for knee OA but no pharmacologic treatment was conditionally
recommended for hip OA, partly because of lack of hip-specific RCTs. <sup>18</sup>

Box 1. Recommendations of National Organizations on Usefulness of Hip and Knee Intraarticular Corticosteroid Injections

Organization	Knee	Hip
American College of Rheumatology	Recommended	Recommended
American Academy of Orthopedic Surgeons	Could be considered	Could provide short-
		term relief
European League Against Rheumatism	Recommended	May be considered
Osteoarthritis Research Society International	<b>Conditionally</b>	Not commented
	recommended	

### **General statements and contraindications for IACS**

IACS are usually injected with local anesthetic. One study compared local anesthetic

with or without methylprednisolone in patients with lateral epicondylitis.<sup>19</sup> The recovery rate, in

terms of pain relief and recovery of function, was significantly better in the corticosteroid and

local anesthetic group throughout the 12-week follow-up.

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The absolute and relative contraindications to intra-articular and soft tissue corticosteroi
injections are listed in <b>Box 2</b> .
Box 2. Absolute and Relative Contraindications to Intraarticular and Soft Tissue
Corticosteroid Injections
Absolute contraindications
Overlying skin infection
(Suspected) infectious arthritis
Fracture site
(Suspected) Bacteremia
Hypersensitivity or allergic reactions to previous corticosteroid injectates
Relative contraindications
Previous lack of efficacy
Severely immunocompromised status
Coagulopathy
Joint prosthesis
Poorly controlled diabetes

### **Choice of corticosteroid for intra-articular joint injections**

There is little evidence to guide selection of one IACS over another. A 1994 survey of the

ACR membership, with 62% response rate reported that 87% of respondents used either

methylprednisolone acetate (MPA), triamcinolone hexacetonide (TH) or triamcinolone acetonide

(TA).<sup>20</sup> The authors noted a strong correlation for type of corticosteroid selected with the region

where the respondent had trained, with MPA in the mid-Atlantic, New England, and the

Southeast; TH in the Midwest and Southwest; and TA in the West.<sup>20</sup>

### **Observational and retrospective studies comparing triamcinolone acetonide and triamcinolone hexacetonide**

In a retrospective study of 85 patients with juvenile RA, 227 joint injections, time to relapse, as assessed by the attending physician was analyzed using Cox proportional hazards <u>model</u>.<sup>21</sup> Doses were standardized by joint. Mean time to relapse was shorter for TA than TH injected joints, 8 vs. 10 months, (P < .0001).

In a prospective study, patients with oligoarticular juvenile idiopathic arthritis, 115 knees and 15 ankles from 85 patients were treated with 1 mg/kg of either TH (n = 70) or TA (n = 60) based on drug availability.<sup>22</sup> The patients were similar based on age, disease duration, gender, antinuclear antibodies (ANA) positivity, type of joint, inflammatory markers and current meds. Patients treated with TA relapsed sooner than patients treated with TH when analyzed by either Cox proportional hazard (hazard risk ratio, 2.7) or time point (6-, 12-, 24-months) with risk rate of relapse approximately 2 for the different timepoints. All results were statistically significant.

### Randomized controlled trials comparing different corticosteroids

In a small study on knee OA, 57 patients were randomized to either TH 20 mg or MPA 40 mg.<sup>23</sup> The patients in the TH group had a statistically greater reduction in pain (visual analog scale – VAS) than did the MPA group at week 3. The authors concluded that MPA was slower in onset and less efficacious than triamcinolone hexacetonide. No differences between the groups were noted as assessed by the Lequesne index, a questionnaire that assesses pain, walking distance, and difficulties of daily life. A review noted that triamcinolone hexacetonide may be associated with faster onset but there were no significant differences in long-term outcomes.<sup>24</sup>

In another small single-blind study, 42 patients with knee OA were randomized to either TH 20 mg or the combination of 6 mg betamethasone acetate and betamethasone disodium phosphate.<sup>25</sup> Triamcinolone hexacetonide had superior clinical benefits at week 1. Treatment failure, defined as a patient's need for a new injection or other therapy, was more common in the betamethasone group (n = 12) vs. the TH group (n = 5).

In a randomized study, one-hundred patients with inflammatory knee arthritis (89 with RA) were randomized to receive either TA 80 mg or MPA 80 mg.<sup>26</sup> No differences were noted in the time to relapse, pain, swelling, range of movement or adverse effects at 4-, 12- or 24-weeks

after the treatments. Research to date has not demonstrated long term superiority of one corticosteroid preparation for IA knee injections

### **Extended-release corticosteroid preparations**

TA extended release preparation results in steadier, longer triamcinolone plasma levels (lasting weeks rather than days) than TA.<sup>27,28</sup> A Phase 2b report studied TA extended release 32 mg vs. TA extended release 16 mg vs. placebo (approximately 100 per group) in patients with knee OA.<sup>29</sup> Although the primary endpoint (average daily pain intensity) was not met, secondary endpoints (improvement in average daily pain) were met, and trends favored the extended release 32 mg dose group. A separate Phase 3 study compared 1:1:1 randomized trial of knee IACS: TA extended release 32 mg vs. TA 40 mg vs. placebo (approximately 161 subjects per group). For Average Daily Pain (primary endpoint), TA extended release was superior to placebo, but no different than TA 40 mg. Secondary and exploratory clinical endpoints favored the extended-release preparation but not significantly.<sup>30</sup>

In a small Phase 2 study, 32 patients with knee OA and diabetes were randomized to either TA extended release 32 mg vs. TA 40 mg and underwent blood glucose monitoring.<sup>31</sup> Patients receiving the extended release preparation mg had statistically and clinically meaningful lower blood glucose during the 48 hours post IACS injection. A review noted that\_TA-ER provides longer plasma levels and less alterations in blood glucose than TA.<sup>24</sup>

It should be noted that studies of TA extended release IACS have been limited to knee and glenohumeral joint injections and funded by the drug manufacturer; whether the results apply to other joints has not been studied at this time. For Statements and Recommendations on corticosteroid pharmacology and AEs in IACS, see **Table 3**.

### Pharmacokinetic and pharmacodynamic studies of IACS injections

Pharmacokinetic studies were done after knee and glenohumeral joint injections. A pharmacokinetic study after knee IACS<sup>27</sup> compared TA with TA-ER. They showed the median time to achieve peak plasma concentration ( $T_{max}$ ) of triamcinolone after TA injection to be 6.5 (range 2, 360) hours and the median terminal half-life ( $T_{1/2}$ ) to be 663.8 (range 18, 2067) hours (663 hours = 27 days) after knee IACS. Another pharmacokinetic study looked at the triamcinolone levels after knee IACS injection of extended release TA.<sup>28</sup> One study showed maximum synovial fluid concentration at week 1, when the sample was obtained, and maximum plasma levels at 24 hours that declined over weeks 6-12 for synovial fluid and weeks12-20 for plasma levels.<sup>28</sup>

Another pharmacokinetic study compared standard TA with an extended release form after glenohumeral joint IACS.<sup>32</sup> Lower peak levels and systemic levels of TA were noted after TA-ER compared to TA. For TA, the  $t_{max}$  was 4 (1–57 hours) (median, range) and remained very high at three to five days after which it declined. The  $t_{(1/2)}$  was 613 (287–1026) hours.<sup>32</sup> It should be noted that the plasma levels remained high up to day 15;  $T_{1/2}$  ranged from 287 (12 days) to 1026 hours (42 days); and duration of measurable plasma levels was 839 hours (35 days).

Regarding pain relief after knee IACS, a study noted relief at one week that extended up to their 12-week follow-up, with both immediate-release triamcinolone and extended-release triamcinolone acetonide.<sup>33</sup> The above studies suggest that pain relief from IACS injections can last from a few weeks, up to 3 months.

For Statements and Recommendations on corticosteroid pharmacology and AEs in IACS, see Table 3.

Choice o	<del>f Corticosteroid</del>
Statemen	
1. The 3 1	nost used corticosteroid preparations for intra articular injection are methylprednisolone
acetate, ti	riamcinolone hexacetonide and triamcinolone acetonide.
Level of e	vertainty: Moderate
2. Variou	s corticosteroid preparations have similar effectiveness but may differ in their duration of
action.	
Level of e	<del>vertainty: Moderate</del>
3. Extend	ed release (ER) corticosteroid preparations have not demonstrated clinical superiority to
	preparations except for improved blood glucose stability in diabetic populations.
	ertainty: Moderate
Recomme	endation
1. There i	s insufficient evidence to recommend one preparation of intra articular corticosteroid over
another.	
<del>Grade I</del>	
Relief fre	om corticosteroid injections
Statemen	ŧ
1. Cortice	esteroid joint injections can provide short term pain relief and improvement in function.
	ertainty: Moderate
Recomme	
1. Cortice	osteroid joint injections can be utilized for short term relief in patients with symptomatic
	tory or degenerative arthritis.
Grade C	

### Frequency of injections and cumulative dose: Results of survey of orthopedic surgeons

The optimal frequency and the total number of corticosteroid joint injections for OA continues to be controversial. An American Association of Hip and Knee Surgeons survey of common injection practices yielded 537 members responses.<sup>34</sup> Most used a 3-month minimum interval between repeat IACS in the same joint, although some respondents preferred a longer interval. The survey showed a great variability in the number of injections allowed per year. Based on the available pharmacokinetic and pharmacodynamic data,<sup>27,28,32,33</sup> we suggest a *minimum* interval of 2-3 weeks, up to three months. The series of injections should be stopped when there is complete or acceptable pain relief or when the relief has plateaued, taking into consideration the maximum cumulative dose. Similar to other injections, the decision when to repeat the injection is between the patient and the physician, taking into consideration the pain

and quality of life of the patient and specific patient characteristics that may put them at higher risk for adverse events.

Injections prior to a planned orthopedic surgery were common. Almost all responders used a local anesthetic mixture with the corticosteroid injection. There were no distinctly defined yearly or lifetime limits. There was a strong consensus for a 3-month corticosteroid-free preoperative interval. There was a near consensus that the efficacy of serial injections decreases over time (as arthritis progresses).<sup>34</sup>

## Landmark-based techniques, role of fluoroscopy and ultrasound: General

### <del>comments</del>

Studies indicate that a landmark injection technique may be sufficient for accurate trochanteric bursa injections and that subacromial subdeltoid bursa (SASDB) injections have been performed under landmark guidance. Some investigators advised that image-guided injections should be reserved for diagnostic arthrocentesis or for cases where complication risk is higher, for example in morbidly obese patients,<sup>35</sup> patients on anticoagulants, or after a previous landmark-based injection or aspiration failure.<sup>35,36</sup> In contrast, the accuracy of landmark-assisted glenohumeral, acromioclavicular joint and SASDB injections has been questioned (see sections on glenohumeral and SASDB injections).

Our literature search did not show a study that compared fluoroscopy with landmarkbased injection. Overall, studies showed improved accuracy of US-guided over landmark-based injections. One review showed US to have improved accuracy over fluoroscopy in glenohumeral joint injections, but it did not reach statistical significance.<sup>37</sup> Two other studies showed comparable results in accuracy, pain relief and functional outcomes between ultrasound-guided

and fluoroscopy-guided glenohumeral joint injections.<sup>38,39</sup>\_A study showed significantly better accuracy with US compared to fluoroscopy in injections around the long head of the biceps but there were no differences in pain relief or complications.<sup>40</sup>

### Accuracy and outcomes of US-guided corticosteroid joint injections

Studies on the accuracy and outcomes of landmark and image-guided injections are discussed in the specific joint sections; studies that involved several joints are discussed here. A randomized controlled trial (RCT) compared ultrasound (US) with landmark based injection in the wrist, hand, or ankle of 114 patients with chronic inflammatory arthritis including RA, psoriatic arthritis, or other spondyloarthritis.<sup>44</sup> The study showed better short term outcomes, measured by functional and clinical scores, with the use of US guidance. A separate RCT of 184 patients with similar chronic inflammatory arthritis across shoulder, elbow, wrist, knee, and ankle found that US guided injections had higher accuracy but showed similar clinical outcomes.<sup>42</sup>

A systematic review of 17 studies confirmed greater accuracy of US-guided IACS, compared to anatomic guidance, into the shoulder, elbow, wrist, hip, knee, or ankle joints <u>and</u> demonstrated better short-term clinical outcomes.<sup>43</sup>-However, there were no differences in longterm outcome measures with either technique. A recent review noted increased accuracy of USguided injections regardless of location, with exception of the hip (due to a lack of comparative studies).<sup>44</sup>

For Statements and Recommendations on the role of imaging in IACS, see **Table 4**. Discussions supporting the Statements and Recommendations on the role of imaging are noted in the section on specific joints.

### Table 4. Statements and Recommendations on the Role of Imaging in IntraarticularCorticosteroid Injections

Role of imaging Statements 1. Ultrasound guided techniques result in more accurate intraarticular needle placement than landmark based techniques. Level of certainty: High 2. There are no significant differences in accuracy between ultrasound guided and fluoroscopy guided peripheral joint corticosteroid injections. Level of certainty: Low 3. Compared to landmark based techniques, use of image guidance may be associated with less pain on injection, improved patient satisfaction and better short term clinical outcomes. Level of certainty: Low 4. Use of imaging guidance may be associated with fewer adverse events, including damage to osteum and intravascular injection, after diagnostic or therapeutic arthrocentesis. Level of certainty: Low **Recommendation** 1. Image guided techniques may be preferred for accuracy of intraarticular corticosteroid injections, especially in morbidly obese individuals. Grade C

### **Chronic shoulder joint pain: Etiologies**

The shoulder joint consists of the primary articulations of the acromioelavicular joint, between the clavicle and the acromion of the scapula; the glenohumeral joint, between the glenoid cavity of the scapula and the humerus; and the scapulothoracic articulation. The etiologies of chronic shoulder pain include acromioelavicular glenohumeral and osteoarthritis, rotator cuff disorders, adhesive capsulitis, and instability.<sup>45</sup>

### Acromioclavicular osteoarthritis

The clinical presentation of acromioclavicular joint OA includes superior shoulder pain, joint tenderness, and a painful body cross adduction test. In the body cross test, the affected arm is elevated to 90 degrees; pain is reproduced in the acromioclavicular joint when the examiner takes the patient's elbow and adducts the arm across the body.<sup>46</sup> Patients with acromioclavicular OA usually present as gradual pain and loss of motion or a history of dislocation or subluxation.<sup>45</sup> – Imaging studies are indicated when diagnosis is not clear. MRI shows

degenerative changes in the joint, osteophytes and or hypertrophy of the clavicle and acromion, and joint edema.<sup>47</sup> As noted previously, IACS is recommended when there is no improvement with the initial conservative management.<sup>48</sup> Non-surgical management includes suprascapular nerve blocks.<sup>49</sup> There has been no dose-response study on IACS for the AC joint, although a dose of 40 mg MP has been injected under fluoroscopy.<sup>46</sup>

### Adhesive capsulitis and glenohumeral joint disease

Disorders of and around the glenohumeral joint is multifactorial, results in frequent shoulder pain, with a lifetime prevalence as high as 67%, and significant functional impairment during and long after the initial painful episode.<sup>50</sup>

Adhesive capsulitis (AC, "frozen shoulder") is a syndrome thought to involve the capsule of the glenohumeral joint, featuring characteristics of shoulder pain, stiffness with reduced range of active and passive motion, and otherwise negative radiographic findings.<sup>54</sup> ACs has been proposed to be a fibroproliferative disease<sup>52</sup> and may be either idiopathic or associated with trauma, tear, surgery, immobilization, or medical diseases (such as diabetes, stroke, thyroid disorders, or Parkinson's). Treatments include conservative analgesic management, physical therapy (PT), short-wave diathermy, IACS, intracapsular hydrodistension, manipulation under anesthesia, and arthroscopic release.

Glenohumeral instability is caused by trauma, repetitive motion of the shoulder (e.g. throwing), high demand shoulder activities (e.g., push-ups, bench presses), or loose ligaments leading to chronic shoulder instability. Treatment is conservative;<sup>48,53</sup> surgery is performed in recalcitrant cases.<sup>54</sup>

Tendinitis of the long head of the biceps

The long head of the biceps tendon is susceptible to trauma, instability, impingement, inflammation of the tendon sheath, instability, and degeneration, resulting in anterior shoulder pain. Patients with biceps tendinitis or tendinosis complain of a deep, throbbing ache in the anterior shoulder.<sup>55</sup> Repetitive overhead motion of the arm initiates or exacerbates the symptoms. A common isolated finding in biceps tendinitis is tenderness over the bicipital groove with the arm in 10 degrees of internal rotation.<sup>55</sup> Tests to diagnose tendinitis of the long head of the biceps include the Speed, Vergason, and upper cut tests. These maneuvers are considered positive when pain is elicited in the bicipital grove. A comparison of the tests concluded that the upper cut test should be used as the screening test and the Speed and Vergason tests as confirmatory tests for confirming disorders of the biceps tendon.<sup>56</sup> MRI can help differentiate between an isolated tear or inflammation of the biceps tendon and other shoulder pathology.

Similar to other causes of shoulder pain, treatment is conservative: rest, medications and physical therapy. Patients with tendinitis and tenosynovitis who do not respond to conservative treatment may benefit from US-guided corticosteroid injections into the biceps tendon sheath.

### Scapulothoracic bursitis

Symptomatic scapulothoracic disorders include scapulothoracic crepitus and scapulothoracic bursitis, collectively called "snapping scapula syndrome."<sup>57</sup> Scapulothoracic crepitus is disruption of the normal gliding of the scapula over the thorax; inflammation of the bursa occurs when there is repetitive movement of the scapula over the thoracic wall (e.g. baseball, swimming). Plain x-ray may show osseous lesions while CT or MRI reveal bursitis. Treatment is conservative,<sup>58,59</sup> with NSAIDS, activity modification and rehabilitation. Landmark scapulothoracic bursa injection, between the servatus anterior and the lateral chest wall, has been

described.<sup>60,61</sup> Surgery includes removal of masses or impinging osseous lesions, bursectomy, or scapulothoracic fusion.<sup>57,59,62</sup>

### **Shoulder corticosteroid injections**

The nonsurgical treatment of persistent shoulder pain is similar regardless of the etiology.<sup>48,49,63,64</sup> The initial treatment consists of activity modification and oral medications including non-steroidal anti-inflammatory drugs, acetaminophen, corticosteroids, antidepressants, and opioids.<sup>48,49,63,64</sup> If there is no relief, heat modalities and physical therapy focused on the specific etiology is instituted.

Injections of the shoulder are for either general shoulder pain or more specifically, adhesive capsulitis, rotator cuff disease/subacromial bursitis, osteoarthritis of the glenohumeral and acromioclavicular joints, tendinitis of the long head of the biceps tendon, and for scapulothoracic disorders.

### IACS and subacromial subdeltoid bursa (SASDB) corticosteroid injection

CSI for shoulder pain can be intraarticular (IA) or subacromial (in or around the subacromial subdeltoid bursa). IACS are done for acromioclavicular and glenohumeral joint pain and ACs while SASDB are usually conducted for subacromial bursitis, rotator cuff disorders, and/or impingement syndrome (**Figure 1**).<sup>65</sup>

The location target for CSI (IACS vs. SASDB) for treatment of ACs has been studied. Chen et al conducted a meta-analysis of 7 articles comparing IACS to SASDB for frozen shoulder and found that IACS reduced pain to a greater degree for up to 3 months compared to SASDB injection.<sup>66</sup> A review and a meta-analysis observed no difference between the two approaches and recommended that either approach can be used for ACs.<sup>65,67</sup>

In an RCT of 58 subjects with moderate to severe post stroke shoulder pain and associated rotator cuff or biceps tendon disease, SASDB injection with corticosteroid conferred pain relief and ROM improvement in shoulder flexion for up to 8 weeks compared with lidocaine.<sup>68</sup>

### Acromioclavicular and glenohumeral IACS: Image-guided vs. landmark guidance

A retrospective study showed that IACS US guided (USG) injection for the treatment of painful acromioclavicular joint due to OA produced better pain and function outcomes than did landmark-guided IACS at 6-months.<sup>69</sup> A 2012 Cochrane review on shoulder IACS that included a meta-analysis of RCTs and non-randomized controlled trials showed better pain outcomes at 6 weeks with image-guided (US) over landmark-guided injections in 3 out of 5 trials.<sup>70</sup> However, the difference was no longer significant when trials with inadequate blinding and allocation concealment were removed.<sup>70</sup> A recent double-blind RCT between USG and landmark-guided injections for adhesive capsulitis did not show difference in pain or functional outcomes despite greater accuracy of the USG injections.<sup>71</sup> This was confirmed in another study.<sup>37</sup>

For glenohumeral joint injections, there have been issues on the accuracy of landmark guidance.<sup>72</sup> For this reason, IACS injection into the glenohumeral joint under fluoroscopy was recommended.<sup>48</sup> One review showed US to have improved accuracy over fluoroscopy in glenohumeral joint injections, but it did not reach statistical significance.<sup>37</sup> Two other studies noted comparable results in accuracy, pain relief and functional outcomes between ultrasound-guided and fluoroscopy guided glenohumeral joint injections.<sup>38,39</sup>

### Subacromial subdeltoid bursa (SASDB)\_corticosteroid injections: landmark approaches

SASDB injections using landmark approaches can be administered via an anterior, lateral, or posterior approaches. A RCT including 50 subjects evaluating landmark based midlateral, a variant of the lateral approach, versus posterior subacromial approach conferred greater accuracy for mid-lateral (92% versus 68%) but there was no difference in functional clinical outcomes.<sup>73</sup> A similar RCT in 80 subjects with subacromial impingement syndrome showed no difference in Shoulder Pain and Disability Index (SPADI), night pain, or shoulder function for up to 12 weeks between posterior vs. lateral approaches.<sup>74</sup> These results were confirmed in a review of 5 RCTs and 3 trials; however, they did not determine superiority of specific approaches in subacromial impingement syndrome.<sup>75</sup>

### US-guided versus landmark injection subacromial subdeltoid bursa (SASDB) corticosteroid injections

SASDB may require less precision in view of its size (largest bursa in the body) and the superficial location of the subacromial space. A study showed similar accuracy between landmark and US-guided SASDB injections; the injection was located in the bursa in all cases. However, the injections were performed by either an experienced orthopedie surgeon or an experienced musculoskeletal radiologist.<sup>36</sup> A study questioned the accuracy of landmark techniques.<sup>76</sup> In this study, the investigators noted 76% (13 of 33 patients) accuracy with the posterior approach and 69% (10 of 33) accuracy with the anteromedial approach.<sup>76</sup> Most important, only the injection into the SASDB resulted in a significant reduction of pain and an improvement in the functional scores.

Two reviews compared the outcomes of USG vs. landmarked based SASDB injection.<sup>77,78</sup> Some analyses favored USG based on 4-week outcomes.<sup>77,79</sup> A 2015 review of

seven papers (445 patients) showed significantly greater improvement in pain and function with USG.<sup>77</sup> Such improved efficacy was not shown in a 2020 review of four papers (234 patients).<sup>78</sup> Some of the differences were based on study selection, but differences were also due to interpretation of the data. Analyses were complicated by multiple study outcomes (pain, function, range of motion [ROM], or other global scores), heterogeneity across studies, and greater risk of bias (for the more inclusive meta-analyses). The sample sizes of all the primary RCTs included were small (fewer than 50 subjects per group).

Two other reviews on USG versus landmark injections looked at papers that included both SASDB and IACS. One group noted that while there was a statistically significant improvement, the clinical benefit was questionable and may not represent "clinically useful differences"<sup>80</sup>; the other group showed a benefit for USG .<sup>78</sup> Overall, the studies showed that accuracy improved with US guided injections, compared to landmark approaches in SASDB and IACS injections.

### **Dose-response studies after shoulder IACS and SASDB injections**

A RCT in 60 patients with full thickness rotator cuff tears compared a single IACS of TA 40 mg (one vs. two vs. no injections), 21 days apart.<sup>54</sup> Night pain and activity related pain were improved among the CSI groups at 1 and 3 months. Longer term Constant Murley shoulder score (a scale that assesses shoulder function based on pain activities of daily living, strength, and range of motion) was similar with treatment vs. no treatment at 3-6 months. The twoinjection steroid dose provided no benefit over the single dose injection.

A RCT showed no difference in efficacy, measured by Shoulder Pain and Disability Index (SPADI) between 20 mg, 40 mg, or 80 mg TA IACS into the glenohumeral joint; all doses showed a reduction of SPADI at the 6-month follow-up.<sup>81</sup>

There is limited evidence on the use of biologic agents and inconclusive results for hyaluronic acid in glenohumeral joint injections.<sup>64</sup>

Two RCTs on IACS for adhesive capsulitis and shoulder joint stiffness showed no difference between 20 mg and 40 mg triamcinolone acetonide.<sup>82,83</sup> In one triple-blind placebocontrolled study in patients with adhesive capsulitis, the two doses were noted to be equally effective in terms of SPADI, VAS, and ROM at the shoulder up to the 12 week follow-up of the study.<sup>82</sup> Another RCT showed equal efficacy between the two doses in patients with shoulder stiffness.<sup>83</sup> Measures included VAS, ROM and the American Shoulder and Elbow Surgeons score; relief lasted up to the 12 month follow-up.

Another RCT of 79 subjects with primary OA and full thickness rotator cuff tear compared USG SASDB injection using TA 20 mg vs. TA 40 mg vs. placebo with follow-up at 8 weeks.<sup>84</sup> The SASDB injections improved pain VAS and active ROM for both doses over placebo throughout the study, but no difference between the TA doses.

In another RCT of SASDB for shoulder pain, 62 subjects were randomized to 1 of 4 groups by preparation (MPA vs. TA) and dose (20 mg vs. 40 mg). All groups pain and function improved from baseline, but there were no differences between any of the 4 groups by either preparation or dose.<sup>85</sup>

A systematic review showed equal efficacy between NSAID and corticosteroid in SASDB injections.<sup>86</sup>

### **Biceps tendon sheath injection**

A study showed that as much of 43% of patients with anterior shoulder pain presumed to have originated from the biceps tendon had normally appearing biceps tendon.<sup>87</sup> The others had tendinosis, tenosynovitis or both, or tendon tear.

A RCT noted the accuracy (location of contrast in the tendon sheath confirmed by CT) of US-guided to be 87% compared to 27% for landmark technique.<sup>88</sup> Another RCT showed significantly better pain relief with US-guided injection than "free-hand injection" without US, and significantly greater improvement in the Constant-Murley score at 31 to 34 weeks followup.<sup>89</sup> A later RCT compared the superior accuracy of US over palpation guided injection into the bicipital grove (100% vs 68%) with less discomfort.<sup>90</sup> Pain relief and improvement in QuickDASH scores at the 4 weeks and 6 months follow-up were significantly better with US. An additional benefit of US is that it permits visualization of the anterior circumflex artery in proximity to the tendon and potentially avoid it.

Fluoroscopy-guided injections were noted to be effective in relieving the pain from biceps tendinitis.<sup>94</sup> However, this retrospective study only looked at six patients. US was noted to be more accurate than fluoroscopy-guided biceps tendon sheath injection. A 10-year retrospective review noted that the first-pass rate (91% for US vs 74% for fluoroscopy), and final-pass rate (98% vs 90%) was better for US, with no difference in pain relief or complications.<sup>40</sup> An additional benefit of US is visualization of abnormalities of the biceps tendon.

The commonly used doses are triamcinolone 40 mg in 9 mL bupivacaine<sup>90</sup> or 40 mg TA in 1 mL lidocaine (reduced to 20 mg in patients with diabetes).<sup>89</sup> There are no dose-response studies.

Biceps tendon rupture is usually due to degenerative changes and to trauma.<sup>92</sup> Tendon rupture can be a consequence of CSI (see section on adverse events).<sup>92-94</sup> Interestingly, peritendinous CSI has been used as treatment for partial biceps tendon tear.<sup>92</sup> Vardakas et al described 7 cases of partial tear, 4 of the 7 had "at least one injection of steroid" as treatment. They did not state the effect of CSI but rather discussed the surgical technique that followed.<sup>92</sup> Lee et al discussed 21 patients with biceps tendinitis and partial rupture who were treated with CSI (US guided injection of TA 40 mg in 1 mL NS & 2 mg ropivacaine into the tendon sheath): 10 patients with biceps tendinosis had good to excellent results while three patients with partial tear had good to excellent results.<sup>95</sup>

### Scapulothoracic bursa injection

Landmark scapulothoracic bursa injections have been described. The patient is prone position and the affected arm in a position of extension, internal rotation, and adduction, and attempting to reach the upper spine, i.e. "chicken wing" position.<sup>60,61</sup> The spinal needle is inserted midway between the spine of the scapula and the inferior angle of the scapula and 3 to 4 fingerbreadths from the vertebral border of the scapula. This is not frequently done because of the risk of pneumothorax. A US-guided subscapularis muscle injection has been described, with the insertion site at the lateral border of the scapula.<sup>64</sup> TA 40 mg subscapularis muscle injection provided equal relief for up to three months, compared to subscapularis bursa injection. Either TA 40 mg in 4 mL lidocaine, or TA 40 mg plus hyaluronate resulted in significant relief of pain of up to three months.<sup>60,61</sup>

# Comparison of corticosteroid (CSI) vs. other therapeutic modalities or agents in shoulder injections

A meta-analysis of single CSI vs. conservative management with non-steroidal antiinflammatory drugs (NSAIDS) for shoulder pain (ACs, subacromial impingement syndrome, nonspecific pain, tendinitis) was performed and included 8 RCTs involving 465 subjects.<sup>96</sup> CSI showed favorable benefit over NSAIDs for improved function (Disabilities of the Arm, Shoulder, and Hand [DASH] and Oxford Shoulder Score) at 4-6 weeks, (primarily seen for ACs and painful shoulder rather than shoulder impingement) but no benefit in pain relief. No differences in complication rates were noted.<sup>96</sup>

A meta-analysis including 6 RCTs (301 subjects) compared CSI with platelet rich plasma (PRP) for pain associated with rotator cuff lesions (tears, tendinosis, impingement) finding shortterm (3-6 weeks) benefit in pain relief and function for the CSI group, but similarly no clinical differences at either intermediate (8-12 weeks) or long-term outcomes (over 12 weeks).<sup>97</sup>

A review and meta-analysis of 3 studies noted that, in patients with subacromial impingement syndrome, SASDB conferred short-term functional improvement compared to PT at 6-7 weeks, but otherwise there were no differences in pain, function or ROM up to 12 months.<sup>98</sup> However, there may be an additive benefit of combining PT, (specifically resistance band training) to SASDB to improve ROM and reduce the need for retreatment of subacromial bursitis after SACS.<sup>99</sup>

#### Adverse effects (AEs) of shoulder corticosteroid injections

A review of RCTs evaluating guidance based shoulder CSI directed to the glenohumeral joint, the subacromial subdeltoid space, or tendon sheaths compared landmark-guided versus

image-guided (fluoroscopy or ultrasound). There was a trend towards lower AEs (all mild) for image-guided CSI, though not significant.<sup>79</sup>

In 1979, 13 cases of tendon rupture after injection of corticosteroids, seven of which involved the long head of the biceps.<sup>93</sup> Triamcinolone 40 mg in procaine was injected in the cases. The interval from injection to rupture ranged from three days to five months. Treatment was conservative, three required surgical repair.<sup>93</sup> A case report noted the progression of a partial tear of the biceps tendon to complete tear after a <u>palpation guided</u> corticosteroid injection.<sup>94</sup> As noted previously, peritendinous CSI has been reported in patients with partial biceps tendon tear.<sup>92,95</sup>

AEs related to CSIs are discussed in the section on general AEs.

### **Comments**

In this section, we discussed different shoulder injections: IA, subacromial subdeltoid bursa, and biceps tendon sheath. SRs specific to these approaches are made in **Table 5**. General comments, not noted in the SRs, include the following:

Studies and reviews had conflicting results and conclusions. Overall, US improved the accuracy of acromioclavicular and glenohumeral joint, SASDB and biceps tendon sheath injections. This did not translate into better functional outcomes in acromioclavicular joint or SASDB injections.

Peritendinous CSI into the biceps tendon has been reported to be effective in patients with biceps tendinosis and in patients with partial tear of the biceps.

Peritendinous CSI injection is controversial in view of possible tendon rupture when the injection is made into the tendon. For this reason, we did not create a SR. The clinician is advised to make an informed decision with the patient.

There is insufficient data to create a position statement regarding the preferred CSI approach for SASDB injections (anterior, lateral, posterior) to improve pain, function, or safety for painful shoulder disorders.

We suggest a minimum interval of 2-3 weeks, up to three months, between injections. A repeat injection is based on a shared decision between the patient and the physician, balancing the intensity of the recurred pain and the adverse events associated with CSI.

#### **Elbow injections**

# Medial and lateral epicondylitis/epicondylosis

Painful syndromes in the elbow, including lateral epicondylitis/epicondylosis (LE) and medial epicondylitis/epicondylosis (ME) when refractory to conservative management, (including PT), are sometimes treated with CSI. LE, commonly known as "tennis elbow," presents with lateral elbow pain reproduced with extension of the wrist. ME, commonly known as "golfer's elbow," presents with medial elbow pain reproduced with flexion or pronation at the wrist. ME can also be reproduced with provocative maneuvers enhancing this motion or with valgus stress testing.

#### **Injection treatment for lateral epicondylosis**

A study noted similar results in terms of pain relief and functional outcomes after USguided or palpation-guided betamethasone injection of the lateral epicondyle.<sup>400</sup> As noted previously, a study showed significantly better efficacy of combined corticosteroid and local anesthetic, compared to local anesthetic alone, in patients with lateral epicondylitis.<sup>49</sup>

Several systematic reviews have examined CSI for LE.<sup>401-406</sup> An early review found the role of CSI for LE to be mostly inconclusive, but CSI for LE might provide benefit short-term (2-6 weeks) relief.<sup>406</sup> Another early systematic review of CSI for elbow and shoulder tendonits<sup>405</sup> found short-term (<8 weeks) benefit of CSI, without long term benefit compared to pooled other comparators (placebo, PT, NSAIDs). Another review identified 12 studies characterized the findings as indicative of strong support for the efficacy of CSI in the short-term compared to no intervention, NSAIDs, PT, and orthoses.<sup>404</sup> However, CSI were found to be less efficacious, in terms of reduction of pain, than no interventions at 26 and 52 weeks.<sup>404</sup> A review of therapies for LE favored CSI for short-term improvements in pain, function, and global improvement over placebo, local anesthetic, orthoses, PT, and oral anti-inflammatories.<sup>407</sup> However, PT and NSAIDs were more effective in the long term. Furthermore, CSI was associated with more frequent LE recurrence compared to PT alone.<sup>407</sup> A later review identified 10 clinical trials assessing CSI for pain due to lateral epicondylosis, 7 of which were published after 2000. CSI conferred analgesic benefit for up to eight weeks after an injection for LE.<sup>402</sup> Overall, the reviews noted short-term (<8 weeks) relief from CSI.

An RCT (not described in the identified systematic reviews noted above) compared NSAID therapy, PT, and CSI for treatment of 60 patients with LE. Patients receiving PT showed modest improvement in grip strength at 2 weeks and improved pain at 2 weeks and 4 weeks compared to the CSI and NSAID.<sup>108</sup>

A recent RCT compared stretching and splinting therapies, deep friction massage and CSI for the treatment of LE (n = 41) and found improvement (decrease in VAS score) for those patients treated with CSI at 6 and 12 weeks (from 45.4 to 31.4) as well as improvement in grip strength (from 46.7 to 60.5 pounds).<sup>109</sup> However, similar clinical improvement was also seen in

the traditional therapy and deep friction massage groups at early follow-up, with no statistical difference among the steroid, therapy, and massage groups. Neither the CSI nor the stretching and splinting group sustained improvement in VAS score at 6-month follow-up, and only the deep friction massage group experienced improved pain (6.7 to 1.3, P = .002) and function (disability of the arm, shoulder, and hand; DASH – a 30-item questionnaire based on the patient's ability to perform specific activities related to daily living and recreation, and weakness and stiffness of arm, shoulder or hand) score increase from 48.6 to 10.3) at 6-months.

In the studies reviewed above, TA or MPA were mostly used, with betamethasone and dexamethasone utilized in very few investigations. Doses of TA employed the whole range (20, 40, 80 mg), 20 and 40 mg for MP, 6 mg for betamethasone, and 4 mg for dexamethasone. One to 2 mL volumes were injected.

# Corticosteroid injections vs. platelet rich plasma and autologous blood for LE

Other reviews have compared CSI for LE to PRP,<sup>410</sup> and autologous blood. A review and meta-analysis comparing the safety and efficacy of injection of autologous blood products to corticosteroid for the treatment of LE identified a total of 10 studies with 509 patients.<sup>401</sup>–CSI was more effective in the short term, but autologous blood products provide more pain relief and improved function in the intermediate and long term. The study described high recurrence rates of LE following CSI, 72% at 6 weeks and 37% at 6 months.

Another meta-analysis compared CSI to PRP and autologous blood in terms of improved function and pain.<sup>444</sup>-Of the 10 studies analyzed, comparisons between PRP, autologous blood and CSI focused on 3 studies with results from within 2 months. These studies favored PRP and

autologous blood in terms of improved function and pain pressure threshold. However, CSI had a more favorable AE profile compared to autologous blood.<sup>411</sup>

Finally, a meta-analysis showed limited favorability for CSI over PRP in the short-term compared (4-8 weeks), but no difference in the long-term (24 weeks).<sup>110</sup>

# **AEs from CSI in lateral epicondylosis**

Common AEs include post-injection flare, minor rash, transient pain (around 11%), skin atrophy, and depigmentation (4%).<sup>105,107</sup> In one study, the rate of pain following CSI was substantially higher compared with injection of local anesthetic (50% vs. 11%).<sup>412</sup> No serious AEs such as tendon rupture or infection were identified in the reviews. There is a statistically higher risk of local pain and skin reaction after injection of autologous blood compared to CSI but not between PRP and CSI or PRP and autologous blood.<sup>411</sup>

# **Injection for medial epicondylosis**

There is paucity of studies investigating CSI for ME. Injection of 40 mg MPA in 1 mL lidocaine provided better short-term benefit at 6 weeks over lidocaine and saline injection.<sup>113</sup> However, there was no difference in effect at three months and one year. The authors believed that the improvement reflected the natural history of the condition.

# **Intra-articular elbow joint injection**

Pain associated with the elbow joint may be due to OA, RA or crystalline arthopathies.<sup>114,115</sup> Few publications have focused on IACS for the elbow, and there were no pharmacokinetic studies after elbow IACS injections. When the elbow was studied, it was one of several joints included in the study.

# **Injection for olecranon bursitis**

A 2016 RCT evaluated resolution of nonseptic olecranon bursitis comparing 90 patients

randomly assigned to either NSAIDS (and compression bandaging), aspiration, or aspiration

with CSI (N = 90; 40 mg TA in 1 mL lidocaine) for the treatment of nonseptic olecranon

bursitis.<sup>116</sup> The proportions of patients experiencing resolution (by VAS score) by week 4 were

similar among the 3 groups. CSI with aspiration was associated with earliest mean resolution at

2.3 weeks compared to aspiration alone (3.2 weeks) or NSAIDs with compression bandaging

(3.2 weeks). There were no AEs or complications reported.

In summary, CSI confers short-term (up to 8 weeks) pain relief for LE. Further research

is required on the utilization of CSI for ME and olecranon bursitis. For this reason, no SR is

provided for medial epicondylosis. For Statements and Recommendations on IACS in shoulder

and elbow, see Table 5.

# Table 5. Statements and Recommendations on Intraarticular Corticosteroid Injections in Shoulder and Elbow

Shoulder joints

 Statements

 1. Lower corticosteroid doses equivalent to 20 mg triamcinolone or methylprednisolone in IACS and SASDB shoulder injections are equally effective as higher corticosteroid doses.

 Level of certainty: Moderate

2. Corticosteroid injection (CSI) of the shoulder provides short-term improvement (up to 8 weeks) in pain and disability over no treatment or placebo for painful shoulder disorders and should be considered for adhesive capsulitis (AC) and other painful disorders of the shoulder (subacromial subdeltoid impingement syndrome, subacromial subdeltoid bursitis, biceps tendinopathy). *Level of certainty: High* 

3. Physical therapy or home exercise, in conjunction with CSI of the shoulder, is beneficial for painful shoulder disorders, including adhesive capsulitis and subacromial bursitis.

Level of certainty: Moderate

Recommendations

1. The recommended initial CSI can be performed with corticosteroid equivalent not exceeding 20 mg triameinolone or methylprednisolone.

Grade B

2. Shoulder CSI should be offered for short-term pain relief of moderate-to-severe pain, disability from shoulder impingement syndrome, bursitis, rotator cuff tendonitis, or tendinopathy if no other conservative treatment options are available or successful.

Grade B
3. Physical therapy or home exercises should be offered in conjunction with shoulder CSI.
Grade B
Tendinitis/tendinosis of the long head of the biceps
Statements
1. For biceps tendon injections, US guided injections improve accuracy, pain relief and functional
outcomes compared to landmark techniques.
Level of certainty: High
2. US guided injections provide higher accuracy of injections than fluoroscopy guided injections, with
similar analgesic benefit.
Level of certainty: Low
Recommendations
1. US guidance is recommended over landmark technique for peritendinous injection of the long head
of the biceps.
Grade A
2. Fluoroscopy guidance is recommended over landmark technique for peritendinous injection of the
long head of the biceps.
Grade B
Elbow joint
Statements
1. Extra articular CSI are effective in the short term for treatment of lateral epicondylosis.
Level of certainty: Low
2. There is no evidence to support long term benefit for CSI for epicondylosis compared to
2. There is no evidence to support long term benefit for CSI for epicondylosis compared to conservative management or physical therapy. The long term improvement may reflect the natural
conservative management or physical therapy. The long term improvement may reflect the natural history of the condition.
conservative management or physical therapy. The long term improvement may reflect the natural history of the condition. Level of certainty: Low
conservative management or physical therapy. The long term improvement may reflect the natural history of the condition.
conservative management or physical therapy. The long term improvement may reflect the natural history of the condition. Level of certainty: Low
<ul> <li>conservative management or physical therapy. The long term improvement may reflect the natural history of the condition.</li> <li><i>Level of certainty: Low</i></li> <li>3. For nonseptic olecranon bursitis, aspiration followed by CSI is safe and may result in earlier</li> </ul>
<ul> <li>conservative management or physical therapy. The long term improvement may reflect the natural history of the condition.</li> <li>Level of certainty: Low</li> <li>3. For nonseptic olecranon bursitis, aspiration followed by CSI is safe and may result in earlier improvement in symptoms compared to aspiration alone or compression with bandaging.</li> <li>Level of certainty: Low</li> <li>Recommendations</li> </ul>
conservative management or physical therapy. The long term improvement may reflect the natural history of the condition.         Level of certainty: Low         3. For nonseptic olecranon bursitis, aspiration followed by CSI is safe and may result in earlier improvement in symptoms compared to aspiration alone or compression with bandaging.         Level of certainty: Low         Recommendations         1. An administration of CSI may be considered for short term treatment of pain due to lateral
<ul> <li>conservative management or physical therapy. The long term improvement may reflect the natural history of the condition.</li> <li>Level of certainty: Low</li> <li>3. For nonseptic olecranon bursitis, aspiration followed by CSI is safe and may result in earlier improvement in symptoms compared to aspiration alone or compression with bandaging.</li> <li>Level of certainty: Low</li> <li>Recommendations</li> </ul>
conservative management or physical therapy. The long term improvement may reflect the natural history of the condition.         Level of certainty: Low         3. For nonseptic olecranon bursitis, aspiration followed by CSI is safe and may result in earlier improvement in symptoms compared to aspiration alone or compression with bandaging.         Level of certainty: Low         Recommendations         1. An administration of CSI may be considered for short term treatment of pain due to lateral epicondylosis unless contraindicated.         Grade C
conservative management or physical therapy. The long term improvement may reflect the natural history of the condition.         Level of certainty: Low         3. For nonseptic olecranon bursitis, aspiration followed by CSI is safe and may result in earlier improvement in symptoms compared to aspiration alone or compression with bandaging.         Level of certainty: Low         Recommendations         1. An administration of CSI may be considered for short term treatment of pain due to lateral epicondylosis unless contraindicated.
conservative management or physical therapy. The long term improvement may reflect the natural history of the condition.         Level of certainty: Low         3. For nonseptic olecranon bursitis, aspiration followed by CSI is safe and may result in earlier improvement in symptoms compared to aspiration alone or compression with bandaging.         Level of certainty: Low         Recommendations         1. An administration of CSI may be considered for short term treatment of pain due to lateral epicondylosis unless contraindicated.         Grade C

# Hip pain

Hip pain is most commonly caused by OA or other inflammatory arthritis (such as auto-

immune or crystalline disease) of the femoral-acetabular joint, and by greater trochanteric pain

syndrome (GTPS). Other reasons for hip pain include osteonecrosis, femoral acetabular

impingement, or labral tear.<sup>117,118</sup> CSIs are used for patients who fail to respond to

pharmacological and non-pharmacological managements, or for patients who are looking for short-term pain relief where hip surgery is either not an option or delayed.<sup>10,18,118-120</sup>

As noted earlier, the recommendations of different organizations regarding IACS into the hip are listed in **Box 1**.<sup>10-12,16-18,121</sup>

# General comments on image-guided hip injections

IACS injections can be performed using landmark technique, fluoroscopy, US or computed tomography (CT).<sup>69,122,123</sup> Fluoroscopically guided hip injections were noted to be more accurate than non-image guided hip injections.<sup>124</sup> For diagnostic purposes only, one study showed comparable accuracy between US-guided and fluoroscopy-guided injections in obtaining arthrography of the hip joint<sup>125</sup> while another study noted similar accuracy, less pain, and better patient preference in US-guided injections.<sup>126</sup> A review noted the absence of comparative data to show increased accuracy with US or x-ray guidance in intraarticular hip injections.<sup>17</sup>

# **Intraarticular hip corticosteroid injections**

A RCT compared 40 mg IACS TH vs. saline (both with bupivacaine).<sup>123</sup> Significant improvements in Western Ontario and McMaster Universities Osteoarthritis (WOMAC, a questionnaire on pain, stiffness, and physical functioning of the joints) index were noted at 1and 2 month follow up for the IACS group. Open-label follow up showed continued improved outcomes at 3 months (but not 6 months). The authors concluded that IA corticosteroid hip injection can be an effective treatment of pain in patients with hip OA, "with benefits lasting up to 3 months in many cases."

Corticosteroid vs. non-corticosteroid anti-inflammatory intraarticular injections

A retrospective comparative study showed no difference in efficacy between IA 40 mg triamcinolone and 30 mg ketorolac in patients with hip OA; the verbal numeric pain scores did not show differences at 1, 3, and 6 months.<sup>127</sup> A double-blind RCT study examined comparative effectiveness of US-guided IACS injection with IA ketorolac injection in patients with symptomatic hip OA.<sup>128</sup> IA injections with either ketorolac or triamcinolone produced significant improvements in patient reported outcome measures largest at 1 week and decreased over time. There were no significant differences between ketorolac and triamcinolone. There were no significant differences between ketorolac could therefore be considered in patients at risk for steroid adverse effects, as a low-cost option.<sup>69,128</sup>

A RCT examined the comparative efficacy of IA hip injections of hyaluronic acid, corticosteroid, and normal saline in patients with hip OA.<sup>429</sup> Patients treated with 40 mg triamcinolone experienced greater improvement 28 days after IACS injection than did patients assigned to the hyaluronic acid group. The outcomes domains were pain on walking and at rest, WOMAC, and Lequesne index. There was no difference in the patients' global assessment of pain. Hyaluronic acid had a considerable effect on patients without effusion but had no effect in the patients with effusion. On the contrary, corticosteroid influenced both patients with and without effusion. The peak effect of the CSI was observed 2 weeks post-injection. The improvement from normal saline injection was insignificant.<sup>429</sup> Another prospective RCT produced a similar result.<sup>430</sup> Patients with hip OA were randomized to one of 4 groups, including non-interventional care (no injection) group, and 3 groups receiving injections: normal saline, hyaluronic acid, and methylprednisolone. The corticosteroid injections were found to be highly efficacious, specifically pain, WOMAC pain and function improved significantly for the steroid group alone.<sup>430</sup> The corticosteroid response was maintained for 8 weeks.

Three systematic reviews compared IACS with placebo (saline), PRP, and hyaluronic acid. The studies were heterogenous in the degree of OA, all trials with different sample sizes, medications used, and timing of follow-up. The most used dose was 40 mg triamcinolone or methylprednisolone. All reviews showed improvement in pain and function with IACS that lasted 4 or 6 months.<sup>131-133</sup> IACS showed better results than hyaluronic acid.<sup>131-133</sup> In a network meta-analysis (with the same above limitations), despite no mean statistical differences across treatments (including saline), IACS was rated as the most favorable treatment by surface under the cumulative ranking curve (a score that represents numeric ranking of treatments, with a greater value indicating greater efficacy) analysis at 2-4 months (both pain and function); whereas HA and PRP had favored rating at 6-months.<sup>133</sup>

Two recent systematic reviews compared the clinical outcomes, in terms of pain and function, between NSAID injection and IACS in hip osteoarthritis. One review noted no difference;<sup>86</sup> both groups showed significant improvement for three to six months. The other concluded that IACS injections were more effective.<sup>134</sup>

#### Volume of injectate and dose of corticosteroid

The reported volumes of IA hip injection vary from 3 mL to 12 mL. In one randomized study, patients were given either 40 mg triamcinolone and 2 mL bupivacaine or 6 mL of sterile water injection. There was no significant statistical or clinical difference in functional scores between the two groups at 3 months. Since there is no detriment to using a larger volume of injectate; the investigators recommended that practitioners use total volumes between 3 and 9 mL.<sup>135</sup>

As noted in the above studies, the <u>most</u> commonly used dose for hip IACS is 40 mg triamcinolone or methylprednisolone.

For Statements and Recommendations on IACS in hip and knee injections, see Table 6.

# Periarticular hip injections: Greater trochanteric bursitis, gluteus tendinopathy, snapping hip syndrome

Greater trochanteric pain syndrome (GTPS) is characterized by pain around the greater trochanter and may radiate distally over the lateral aspect of the thigh. It is more common in women. GTPS can be caused solely or combination of trochanteric bursitis, gluteus medius or minimus tendinopathy, or snapping hip (palpable or audible snapping with active hip motion).<sup>136</sup> The current thinking is that GTPS is mostly caused by gluteal tendinopathy.

#### Greater trochanteric bursitis

There are four bursae around the greater trochanteric prominence: subgluteus maximus bursa, subgluteus medius bursa, subgluteus minimus bursa, and gluteofemoral bursa.<sup>437</sup> The subgluteus maximus bursae, located lateral to the great trochanter is the largest and most incriminated in trochanteric bursitis. Greater trochanteric bursitis is denoted by pain over the buttock and lateral aspect of the thigh that may radiate down the leg to the proximal tibia, at the level of the insertion of the iliotibial tract.<sup>137</sup> The patient has pain when lying on the affected side, pain in the area when climbing or descending stairs or when rising from seated position. Physical examination shows pain on pressure on the greater trochanter; Jump sign is positive (**Box 3**). There is anechoic fluid in the greater trochanter on US.<sup>438</sup> MRI shows high signal intensity of the bursa on fluid sensitive sequences.<sup>437</sup> Greater than 50% relief after CSI (40 mg TA in 6 mL local anesthetic) under US has been used to diagnose trochanteric bursitis.<sup>437</sup> Greater trochanteric bursitis as a cause of GTPS is lower than previously thought. A US study of 877 patients with GTPS noted 50% had gluteal tendinosis, 0.5% with gluteal tendon tears, and 28.5% with thickened iliotibial band. Only 20% had trochanteric bursitis.<sup>438</sup>

#### Gluteus medius/minimus tendinopathy

Gluteus medius/minimus tendinopathy is characterized by lateral hip pain localized to the greater trochanter. There is discomfort with walking and stair climbing and pain lying on the affected side. Signs include tenderness at the greater trochanter and localized lateral hip pain with flexion, abduction, and external rotation (FABER) testing. The hip-lag sign and the Ossendorf and Lequesne tests are positive (**Box 3**). There is pain with resisted hip abduction and with resisted hip internal rotation.<sup>439</sup> MRI (increased signal intensity or tendinitis, soft tissue edema, tear) and ultrasound (tears, absence of tendon fibers, muscle wasting) can document the presence of gluteal tendinopathy and tears.<sup>440</sup>

#### Snapping hip syndrome

Snapping hip syndrome (SNS), also called "coxa saltans," is characterized by a perceptible or audible snap the hip area and maybe accompanied with pain.<sup>141</sup> It occurs in two forms: internal or medial (ISHS) secondary to the iliopsoas tendon movement, and external or lateral (ESHS) commonly due to the iliotibial band.<sup>141</sup>

ISHS is generated by movement of the iliopsoas tendon and an audible snap is noted in the anterior portion of the hip. Etiologies include anatomic variabilities of the iliopsoas tendon, or acetabular cup malposition or anterior protrusion of the screws after THR. Physical examination findings include tenderness to palpation and positive Thomas and Stincfield tests (**Box 3**)<sup>-142,143</sup> Both tests rely on hip flexion and strain the iliopsoas. MRI may show edema around the iliopsoas while US may reveal evidence of tendinopathy (abnormal foci of hypoechogenicity or thickening of the tendon), bursitis (peritendinous fluid collection) and increased blood flow around or within the iliopsoas tendon.<sup>144</sup>

ESHS is more prevalent, characterized by pain in the lateral aspect of the thigh. It is ascribed to the movement of the iliotibial band over the greater trochanter, seen during deep hip flexion or rotation. Etiologies include iliopsoas tightness or bursitis or hypertrophy of the psoas tendon. Tests include the Ober and hula hoop tests (**Box 3**).<sup>141,142,145</sup> MRI may show edema, increased signal, or tears in the iliotibial band. Treatment includes PT, NSAIDs, or corticosteroid injection into the trochanteric bursa.<sup>144</sup> Surgery is performed in refractory cases: release of iliotibial band or endoscopic gluteus maximus tendon release. The proximal iliotibial band syndrome should not be confused with the distal IT band friction syndrome at the knee (see below).

Diagnosis	Test	Description
Greater trochanteric bursitis	Jump sign	Severe sensitivity and intense pain on
		pressure over the most prominent ridge of
		the greater trochanter that the patient wants
		to "jumps off" the bed
Gluteus medius/minimus	FABER test	Ipsilateral hip pain with flexion, abduction,
tendinopathy		and external rotation
	Ossendorf test	Patient in lateral position, knee of the
		tested side is flexed to 45° and the hip
		passively abducted and the leg passively
		elevated by the investigator. The patient is
		asked to bring his knee in the direction of
		the examination table. The test is regarded
		positive, if no internal rotation is possible,
		maneuver is painful, or groin pain is
		elicited.
	Hip lag sign	Patient in lateral position, with affected leg
		up. The examiner positions one arm under
		this leg, whereas the other hand stabilizes
		the pelvis. The hip is passively extended to
		10 degrees, abducted and rotated internally
		as far as possible, while the knee remains
		in a flexed position. The patient is asked to
		hold the leg actively in this position. The
		test is positive if the patient is not able to
		keep the leg in the abducted, internally
		rotated position, and the foot drops more
		than 10 cm.

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Internal snapping hip	Thomas test	Patient lies supine and pulls the unaffected
(iliopsoas tendon/bursa)		knee to the chest, test is positive if patient
		is unable to keep the affected limb fully
		extended on the examination table or feels
		a stretch in the groin.
	Stinefield test	Patient lies supine with hip at 30° and is
		asked to fully flex the hip again resistance;
		test is positive when internal snapping is
		reproduced.
External snapping hip	Ober test	Patient lies on the non-painful side and
(iliotibial band)		raises the knee up and down with the knee
		at a right angle; test is positive when there
		is anterior groin pain with visible or
		audible snapping.
	Hula-hoop test	Patient stands with adduction and
		circumduction of the affected hip; positive
		test is the presence of snap over the greater
		trochanter.

Ossendorf test and Hip Lag Sign are tests of hip abductor muscle (gluteus medius/minimus) tear, rupture, or damage. Thomas test and Stincfield test rely on hip flexion.

#### Use of imaging in periarticular hip injections

Earlier reports suggested that periarticular hip injections (**Figure 2**) can be performed using landmarks, fluoroscopy, or US.<sup>35,146-149</sup> A cadaveric study of 24 hip specimens (<u>BMI</u> unknown) compared the accuracy between landmark-guided and US-guided greater\_trochanteric bursa injections.<sup>450</sup> The accuracies (intrabursal injection) were 67% for landmark vs. 92% for US-guided, with no statistically significant difference (P = .25), though the study may be underpowered to detect a statistical difference. Using landmark guidance, a clinical study showed attainment of a bursagram in 45% of the patients on first attempt, 23% on the second attempt, and 23% on the third attempt.<sup>447</sup> In a subsequent study, the same investigators noted similar positive bursagram and similar functional outcomes (Oswestry scores, SF-36, patient satisfaction) between fluoroscopy and landmark-guided trochanteric bursa corticosteroid injection (60 mg MPA plus 2.5 mL local anesthetic).<sup>148</sup> In obese patients, trochanteric bursa

injections under fluoroscopy significantly reduced immediate and 1-week post-injection pain scores.<sup>151</sup>

There has been no study that compared US and landmark injections; most studies used US guidance, two involved fluoroscopy.<sup>148,151</sup> While studies showed no statistically significant benefit with imaging (fluoroscopy or US), the use of fluoroscopy or US is recommended in obese patients where palpation of the greater trochanter can be difficult or when landmark-based injections have failed.

US-guidance has been recommended for tendon sheath injections and iliopsoas bursa injections.<sup>152</sup> There has been no study that compared landmark with US in gluteus medius/minimus tendon injections. Visualization of the tendon with US is an obvious advantage to prevent intratendon injection and possible rupture.

There has been no study that compared iliopsoas injection with image-guided (US or fluoroscopy) versus landmark-guided. Fluoroscopy-guided iliopsoas bursa corticosteroid injection (TA 40 mg in 5 mL lidocaine) has been described with the center of the acetabular roof as the target area and confirmed by injection of contrast.<sup>153</sup> The study of 39 patients showed 49% had "clinically relevant improvement" at one month follow-up. A cadaver study noted 90% accuracy with US-guided injection, with the injectate covering 50 to 100% of the iliopsoas tendon.<sup>154</sup>

#### **Treatment of GTPS, efficacy of injections**

Treatments of GTPS include physical therapy, analgesics, NSAIDs, injections; surgery is performed in recalcitrant cases.

Trochanteric bursa injection

Small observational studies suggested that local CSI may be beneficial in the management of trochanteric bursitis.<sup>455,156</sup> CSI utilizing 60 mg MPA in 2.5 mL lidocaine, done either with fluoroscopy of landmark, resulted in greater than 50% pain relief at 1 month (61% of patients), 3 months (44% of patients) with perceived positive global effect.<sup>448</sup> TA 20 mg in 3 mL local anesthetic under fluoroscopy significantly reduced the pain at one-week follow up.<sup>454</sup> A review noted that injection in the "greater trochanteric bursa" (they meant the subgluteus maximus bursa specifically) in patients with trochanteric bursitis resulted in longer pain reduction compared to injection into the gluteus medius bursa or extrabursal sites and that imageguided injections resulted in maintained lower pain scores up to six months.<sup>457</sup>

Two randomized trials compared CSI into the greater trochanter with other modalities.<sup>158,159</sup> A RCT showed CSI (25 mg prednisolone in 4 mL mepivacaine) into the point of maximal tenderness or swelling in the greater trochanter to be more effective than home training (progressive repetitive exercises) or shock wave therapy at 1 month but not at 4 months or 15 months.<sup>159</sup> Another RCT showed that CSI (40 mg TA in lidocaine) into the point of maximal tenderness in the greater trochanter provided more pain relief at 3 months follow-up than usual care(analgesies, physical therapy) but there was no difference at 12 months.<sup>158</sup>

A randomized double-blind placebo-controlled (normal saline) trial investigated the efficacy of CSI (1 mL betamethasone in 4 mL lidocaine) in greater trochanteric pain syndrome (lateral hip pain reproduced by palpation of the greater trochanter).<sup>160</sup> Under US guidance, the injection was made into either within the peri-trochanteric bursa (if visualized), or at the surface of the distal gluteus medius tendon near its insertion at the postero-lateral facet of the greater trochanter. There was no difference in pain relief after 1 month, although there was a trend

towards improvement in pain scores in favor of the steroid (P = .08). There were no significant differences at 3 or 6 months.<sup>460</sup> The investigators concluded that CSI for trochanteric bursitis is of limited benefit, that glucocorticoid injections are of no greater efficacy than the injection of normal saline solution in patients with GTPS. It is important to note that the injection of saline for trochanteric bursitis is not truly a sham procedure (relief maybe due to washout of inflammatory mediators).

#### Extra-trochanteric bursa injections

Needle manipulation with or without injectate injection or aspiration is one of the treatment options for GTPS. In one study, the diagnosis of GTPS was the presence of pain "anywhere from the iliac crest to the mid-iliotibial band ."<sup>161</sup> This RCT of CSI (80 mg MPA in 8 mL local anesthetic into the point of maximal tenderness in the greater trochanter) vs. dry needling in patients with GTPS showed noninferiority of dry needling for pain and function scores at 6 weeks.<sup>161</sup> In this study, the site of dry needling was determined by the therapist but usually involved trigger points in the gluteus maximus/medius/minimus, piriformis, or tensor fascia lata.<sup>164</sup> Another RCT showed that the efficacy of US guided CSI (80 mg MPA in 7 mL local anesthetic) and extracorporeal shock wave therapy were similar at 3 months, with shock wave therapy being more effective at 12 months.<sup>162</sup> In this study, the inclusion criteria was characteristic of trochanteric bursitis but the injection was made into the "target bursae and tendon insertions."

A recent systematic review and metaanalysis compared CSI with PRP.<sup>136</sup> In the review, studies included both greater trochanteric bursitis and gluteus tendinopathy, and the specific site of injection was not noted in one study. The authors concluded that CSI and PRP are useful options in GTPS and that the superiority of one over the other is not clear.

#### Gluteus medius/minimus tendon injection

A RCT demonstrated that a US-guided intratendinous injection of PRP produced significantly better outcomes (pain and function) than CSI at their 12-week follow-up.<sup>163</sup> Celestone chronodose in saline was injected into the "affected tendon" under US. At 12 weeks follow-up, PRP gave better results (Harris hip score, minimally important clinical difference) than CSI. To determine the duration of pain relief, a study by the same investigators demonstrated that US-guided intratendinous PRP injections produced sustained clinical outcomes at 2 years, whereas the improvement from CSI was maximal at 6 weeks and was not maintained beyond 24 weeks.<sup>164</sup>

A multicenter single blinded RCT on patients with gluteal tendinopathy compared CSI with education on load management plus exercise and a wait and see approach. Either 1 mL betamethasone or 1 mL TA (40 mg) in 2 mL local anesthetic was injected under US into the trochanteric bursa. (Note that the injection was into the trochanteric bursa when the diagnosis was gluteal tendinopathy, although the muscles insert into the superior aspect of the bursa.) Education plus exercise was better than CSI (US-guided bursa injection per published protocol),<sup>165,166</sup> or the no treatment approach at 8 months follow-up. At 52-week follow-up, education plus exercise led to better global improvement, with no difference in pain relief, than CSI.<sup>166</sup>

#### Snapping hip syndrome

Treatment of iliotibial band syndrome includes PT, NSAIDs, or corticosteroid injection into the iliopsoas bursa. Ultrasound-guided corticosteroid injection (TA 40 mg in 4 mL lidocaine) into the iliopsoas bursa resulted in pain relief: 29 of 40 patients (72%) had complete or partial

relief.<sup>144</sup> The authors noted a good correlation between pain relief after CSI with results of surgery (arthroscopic iliopsoas tendon release or arthroscopic debridement of labral tears), with a minimum follow-up of 12 months.<sup>144</sup>

#### Corticosteroid doses

Corticosteroid doses in trochanteric bursa injections were 40 mg TA or MPA, 80 mg TH, or one mL betamethasone.<sup>136,158-160</sup> For injections around the tendons of the gluteus medius or gluteus minimus, doses of 40 mg TA and one mL betamethasone were employed.<sup>165,166</sup> TA 40 mg in 4 mL lidocaine has been injected into the iliopsoas bursa.<sup>144</sup>

# **Comments, Statements and Recommendations for pericapsular hip injections**

In the previously cited studies, the site of pericapsular hip injections was not clear. In some studies, the injection was made into the site of maximal tenderness or swelling, peritrochanteric bursa if visualized or land-mark-guided insertion of the gluteus medius tendon into the greater trochanter, per discretion of the provider (surgeon or physician assistant), or the site of injection was not noted. In one study, the diagnosis was gluteus tendinopathy but the injection was into the trochanteric bursa. This is partly explained by the varied etiologies of pericapsular hip pain and the inclusion of various etiologies in studies. *Owing to this heterogeneity, we are not providing statements or recommendations related to pericapsular hip injections. However, in view of the better efficacy of CSI over home training, usual care, or shock wave therapy shown in some studies, it is reasonable to initiate therapy with CSI in pericapsular hip pain.* 

# **Hiotibial band friction syndrome**

Iliotibial band friction syndrome results from repetitive friction between the iliotibial band and the lateral femoral condyle. It is usually seen in runners and cyclists and has been reported after knee cementoplasty. The syndrome is characterized by lateral knee pain, aggravated by knee flexion and relieved by full knee extension. Treatments include rest, reduced running, NSADs; surgery is performed in refractory cases. A RCT compared CSI with MPA 40 mg with local anesthetic compared with local anesthetic injection into the point of maximal tenderness in the lateral femoral condyle.<sup>467</sup> The decrease in pain during running was significantly better with the CSI at the 7 and 14 days follow up. There were no complications, although only 18 patients were studied.<sup>467</sup> There is a case report of iliotibial band rupture two months after several CSIs (3 CSIs – 40 mg TA in 8 mL local anesthetic) every two months) in a patient with iliotibial band friction syndrome.<sup>468</sup>

#### Knee injections

The recommendations of the different organizations (AAOS, ACR, EULAR, OARSI) regarding knee IACS are noted in **Box 1**.<sup>10 12,16,18</sup>

# Landmark vs. image guided knee injections

A prospective study compared the accuracy of different approaches with the landmarkbased needle IACS into the knee. There was 75% accuracy rate with the anteromedial approach and 93% accuracy rate with the lateral midpatellar approach.<sup>169</sup>

A prospective randomized study examined differences in patient satisfaction, functionality, and the quality of life in adult patients receiving US-guided vs. landmark-guided knee aspiration followed by IA CSL.<sup>170</sup> It was noted that US-guided injections resulted in greater improvement in pain indexes and better patient satisfaction and quality of life scales after 4-6

weeks compared with landmark techniques.<sup>470</sup>-US-guided knee joint aspiration and injection not only resulted in significantly less procedural pain, but also greater synovial fluid yield and more complete joint decompression. The same positive outcome measures, plus improved clinical outcomes were noted in another knee study.<sup>471</sup>-A recent review of 12 published clinical studies, seven of which directly compared US with landmark-guided knee injections, all noted better accuracy with US in each of the 7 studies.<sup>472</sup>

# **Comparative effects of different corticosteroids and dose-response studies**

Studies comparing different corticosteroids, including extended release preparation, were mostly done in knee injections (see "extended release corticosteroid preparations"). As noted earlier, research to date has not demonstrated long term superiority of one corticosteroid preparation for IA knee injections.<sup>24</sup>

#### **Dose-response studies and long-term efficacy of knee IACS**

In a 12-week double-blind RCT, 80 mg of IA TA was compared to 40 mg of TA.<sup>173</sup>-Of the two doses, 80 mg was not found to be superior to 40 mg for IA in terms of pain relief or functional improvement.

Neither IA injections of corticosteroid nor hyaluronic acid provided sustained symptom relief over 2 years.<sup>174</sup> A clinical evidence synopsis concluded, with low quality evidence, that IACS for knee OA may be associated with moderate improvement in pain and a small improvement in physical function up to 6 weeks after injection.<sup>175</sup> A systematic review and metaanalysis confirmed the short-term (up to 6 weeks) superiority of IACS in the knee while longterm follow-up (24 weeks or longer) showed a trend towards superiority of controls (IA hyaluronic acid, IA NSAID, PT).<sup>176</sup> A systematic review of guidelines also noted the short-lived improvement (less than 4 weeks) with IACS into the knee joint.<sup>177</sup> A recent systematic review

noted no difference in outcomes between IACS and NSAID injection into the knee joint, both showed improvement at one and three months.<sup>86</sup>

We previously discussed the pharmacokinetic and pharmacodynamic studies after knee IACS (see "pharmacokinetics and timing of responses"). In summary, pain relief is noted at one to two weeks after injection. Such relief extended to 12 weeks.<sup>33</sup> The timing of these responses coincided with the  $T_{max}$  and  $T_{1/2}$  concentrations of the corticosteroid.<sup>27,28,33</sup> For this reason, we *suggest* follow-up at two weeks to three months, after injection.

# Post-injection protocol to optimize efficacy and safety

After a corticosteroid injection into a joint, it is common for physicians to limit activity to minimize possible chondrotoxic effects, systemic absorption and potentially improve outcome. In a survey, 29% of rheumatologists did not restrict weight bearing after a corticosteroid knee injection while 8% of rheumatologists restricted weight bearing for up to 1 week.<sup>20</sup> In another survey, 42% of respondents recommended avoidance of weight bearing after knee joint steroid injection. There was an increased likelihood that rheumatologists (71%) would recommend limited weight bearing for 1 or 2 days as compared to general practitioners (57%) and orthopedie surgeons (3%).<sup>478</sup> A Cochrane Review found low quality evidence to support splinting/resting a knee in this population after injection, but not the wrist.<sup>479</sup> In one trial, there was significant improvement in pain, stiffness, knee circumference, and walking time in the rested group (no point estimates were provided):<sup>480</sup> In pediatric patients, a retrospective observational study of 2 pediatric hospitals showed no clear benefit of rest/splinting post-injection after knee IACS.<sup>484</sup> In fact, patients who had post-injection splinting had a trend toward more arthritis recurrence (38%  $\frac{v_5 26\%}{P} = .14$ )

#### Adverse events related to knee joint corticosteroid injections

The local adverse effects for the knee include joint destruction, avascular necrosis, and Nicolau syndrome (i.e., variable degrees of skin and underlying tissue necrosis).<sup>182-184</sup> Discussion on cartilage health and systemic adverse events are included in the section of general adverse events.<sup>185</sup>

In summary, US guided IACS knee injections are more efficacious (less procedural pain, greater aspirate volume and better short-term outcomes) than landmark-assisted injections. There is no long-term superiority between the different corticosteroids. Triamcinolone at a dose of 40 mg is as effective as 80 mg. Relief from IACS is short-term (up to 6 weeks). For Statements and Recommendations on IACS in hip and knee joints, see **Table 6**. In view of the pharmacokinetic and pharmacodynamic studies to knee IACS, we suggest a *minimum* 2-week interval between injections.

# Table 6. Statements and Recommendations on Intraarticular Corticosteroid Injections in Hip and Knee Joints

Hip injections Statements

1. Intra articular corticosteroid hip injections are commonly performed procedures that can be utilized as a diagnostic tool in pain due to hip osteoarthritis or as a treatment modality for short term (4-12 weeks) pain relief.

Level of certainty: High

2. Potential adverse effects of standard doses of intra articular corticosteroid hip injections may include accelerated cartilage loss, subchondral insufficiency fractures, osteonecrosis, and rarely rapid joint destruction.

Level of certainty: Moderate

Level of certainty: Low

5. Safety and accuracy of greater trochanteric bursa corticosteroid injections are similar across injections performed using landmarks, fluoroscopy, or US.

<sup>3.</sup> Pre-injection/screening x-ray of the hip joint may help to verify baseline pathology, for example, osteonecrosis with preserved femoral head, that would preclude corticosteroid injection.\* *Level of certainty: Moderate* 

<sup>4.</sup> Education and exercise, in conjunction with IACS, result in better global improvement than IACS alone in patients with greater trochanter pain syndrome at 1 year post intervention. Pain relief is similar after both interventions.

Level of certainty: Moderate
Recommendations
1. Caution should be taken with intra articular hip injections utilizing high dose corticosteroids and
multiple injections. Consider using the lowest effective dose of corticosteroids for IACS of the hip
while extending the time interval between repeat CSI.
Grade B
2. Consider using a 40 mg dose of triamcinolone or comparable dose of another corticosteroid for
intra articular corticosteroid hip injection.
Grade B
3. Pre injection/screening x ray of the hip joint should be performed prior to intra articular
corticosteroid hip injection to verify baseline pathology including osteonecrosis.*
Grade B
4. Patient education and home physical therapy exercises should be offered in conjunction with or prior
to CSI for greater trochanter pain syndrome.
Grade B
5. Hip trochanteric bursa injections can be performed using landmark guidance.
Grade B
Knee injections
Statements
1. The lowest effective dose for triameinolone acetate and methylprednisolone acetate is 40 mg. TA and
MPA are non superior in comparison to each other; both are similarly effective for the clinical
treatment of knee arthritis.
Level of certainty: High
2. Repeat IACS are associated with small volume cartilage loss with the effect likelihood and size
increasing with higher doses and/or extended duration of therapy.*
Level of certainty: High
Level of certainty: High           Recommendations
Recommendations           1. IACS for knee osteoarthritis should use the lowest effective doses of corticosteroids while increasing
Recommendations
Recommendations           1. IACS for knee osteoarthritis should use the lowest effective doses of corticosteroids while increasing the time interval between repeat injections when possible.

Grade A

\*Some of the studies supporting Statements and Recommendations related to harmful developments are discussed in the section on Adverse Events.

# **Small Joints, Wrist and Hand Joints**

#### Wrist and hand corticosteroid injections

CSI of the joints of the wrist, hand and small joints have been reported for treatment of

both inflammatory and noninflammatory arthritis.<sup>186-197</sup> In a prospective open-label study, 30

subjects with RA had ultrasound-guided corticosteroid injections into wrist and/or hand joints,

using 40 mg TA for the wrist joints and 20 mg TA for metacarpophalangeal (MCP) and PIP

joints. There was a statistically significant improvement in visual analog pain scores, swelling, tenderness, synovial hyperplasia and power doppler signal scores at four to 12 weeks postprocedure as compared to baseline for all joints.<sup>187</sup>

While select individual RCTs have shown efficacy of corticosteroids over placebo in IA injections in osteoarthritic interphalangeal joints for treatment of pain, this has not held true when data is analyzed in aggregate.<sup>496</sup> A systematic review of 13 RCTs showed no overall benefit for CSI, over placebo.<sup>495</sup> One trial showed no improvement in pain after corticosteroid injection in the carpometacarpal (CMC) joint for the treatment of OA.<sup>498</sup> Another trial demonstrated significantly less pain during movement, but not at rest, in patients with interphalangeal OA; the authors concluded that this isolated finding requires confirmation.<sup>499</sup> Another systematic review demonstrated with low to moderate quality data that IA saline is superior to CSI in trapeziometacarpal (so called "thumb base") OA when confirmed with radiography using pain and function as endpoints.<sup>497</sup> The ACR provided conditional recommendation for IACS in hand OA.<sup>40</sup>

#### **Beneficial effect of US-guided injection**

The use of US guidance for wrist and hand corticosteroid injections appears to be beneficial.<sup>171,186,187,200</sup>-US-guided IACS into the distal radioulnar joint were significantly more accurate than landmark-guided IACS (100% vs. 75.8%, respectively).<sup>201</sup>-Of note, the study demonstrated no significant difference in clinical outcomes between the US-guided CSI and the landmark injection technique groups.<sup>201</sup>

A metaanalysis of 4 studies comparing US-guided wrist and hand corticosteroid injections to landmark-guided injections showed that the US-guided injection technique was more likely to result in decreased pain and increased function at a 6-week follow up interval.<sup>200</sup>

In one study, US-guided injections for patients with rheumatoid arthritis demonstrated improvement in pain and function as compared to landmark-guided injections and an 8% reduction in cost. It should be noted that in this study, only 3% of the joints injected were "small joints."<sup>188</sup>

#### Post-injection management after wrist injections: Rest versus activity

Unlike knee IACS injection, there appears to be no benefit with rest after wrist injection. A trial noted an increase in relapse rate, with no difference in pain relief, wrist function, grip strength or ROM in the patients who had 48 hours of rest using elastic wrist orthoses, compared to the non-rested group.<sup>202</sup>

#### **Trigger finger**

Stenosing tenosynovitis, known as "trigger finger", is snapping or locking of a finger or thumb, usually at the metacarpophalangeal joint. It is caused by disproportion of the volume of the tendon sheath and its contents, inhibiting the straightforward gliding of the tendon through the digital pulley (structure that holds the tendon against the finger bone). A dose response study showed significantly better results with 20 mg TA compared to 5 and 10 mg at 3 and 6 months of follow-up. However, there were no differences at 9 and 12 months.<sup>203</sup> A 2018 systematic review found moderate evidence for the benefit of CSI in the short term (0-3 months) for the treatment of trigger finger.<sup>204</sup>

A prospective case-control study evaluated US-guided and palpation-guided trigger finger injections with corticosteroids and found no differences at 6 weeks or 6 months in terms of clinical efficacy. There was a significant increase in procedural time and effort with US.<sup>205</sup>

# **De Quervain tenosynovitis**

De Quervain disease is noninflammatory thickening of the ligament overlying the tendons in the first dorsal compartment of the wrist, impeding the gliding of the adductor policis longus and extensor pollicis brevis tendons. This hinders the function of the thumb and produces pain in the thumb side of the wrist. A systematic review evaluating <u>corticosteroid</u> injection vs. placebo and acupuncture for DeQuervain tenosynovitis showed moderate benefit for CSI in the short term (0-3 months). The review also demonstrated that there is moderate evidence that a thumb splint added to a CSI leads to effective treatment in the short- and intermediate term (0-3 and 4-6 months respectively).<sup>204</sup>

#### Plantar fasciitis

The terms "plantar fasciitis," "heel pain," and "plantar heel pain" are often used interchangeably in the medical literature.<sup>206,207</sup> Etiologies include biochemical (extreme pronation of the talar joint), anatomic (flat foot), and chronic disease (diabetes, obesity). Pathophysiology can either be inflammatory, secondary to immune system activation and vasodilatation, or noninflammatory from fibroblastic hypertrophy.<sup>208</sup> Deposition of corticosteroids in or near the origin of the plantar fascia has been utilized as a treatment for plantar heel pain for decades.<sup>209</sup> A 2017 Cochrane Review evaluated 42 studies (36 were RCTs) to assess efficacy of CSI in the treatment of plantar fasciitis. The data supported the use of corticosteroid injections over placebo or no treatment but only up to 1 month.<sup>206</sup> A 2019 systematic review, comprised of 47 trials, concluded that corticosteroid injections for plantar heel pain, was more effective than autologous blood or foot orthoses in reducing pain and more efficacious than PT in improving function, but only in the short term (up to 6 weeks). Notably, CSI was not more effective than placebo in terms of pain relief or in improving function.<sup>207</sup> The

authors noted that in the long term (13-52 weeks), PRP injections and dry needling were superior to corticosteroid injections.<sup>207</sup> The majority of trials were small (mean size 28 subjects) and had significant risk of bias (most frequently due to lack of blinding) resulting in low or very low quality of evidence. Another 2019 systematic review and meta-analysis based on 31 RCTs demonstrated that there was no difference in outcomes for plantar heel pain between corticosteroid injections, oral NSAIDS, therapeutic exercise, orthoses, or extracorporeal shockwave therapy.<sup>210</sup>

An important distinction is the treatment of plantar heel pain associated with rheumatologic inflammatory arthritis, especially spondyloarthritis. Enthesitis, or inflammation, at the site of attachment of tendons and ligaments to bones, is characteristic of spondyloarthritis. A systematic review of the treatment of this subset of plantar heel pain associated with rheumatologic inflammatory diseases included 5 studies. All studies demonstrated efficacy and safety of US-guided corticosteroid injection.<sup>211</sup>

The corticosteroids used in the above studies were methylprednisolone, triamcinolone, betamethasone, and dexamethasone. There were no dose response studies; the doses ranged from 20 to 80 mg for MP and TA, 6 mg for betamethasone and 4 to 8 mg for dexamethasone. In the studies that noted the repeat injections, the interval between injections were 2, 3, and 6 weeks, and three months.<sup>206</sup>

Known complications of plantar fascia injections with corticosteroid include fascial rupture and fat pad atrophy.<sup>206,212,213</sup> A longitudinal cohort study followed 174 patients for 5 to 15 years, wherein the patients received US-guided steroid injections of the plantar fascia for 5 to 15 years. At follow-up, the mean fat pad thickness in the patients who received US-guided CSI

was 9.0 mm (95% confidence interval [CI], 7.0-10.9 mm) compared to 9.4 mm (95% CI 7.2-11.6

mm) in the patients without an injection (P = .66).<sup>209</sup> The decrease in thickness could be due to

age/aging or to the corticosteroid from reduction of the edema secondary to decrease in

inflammation. In this study, no patient suffered a fascial rupture.

For Statements and Recommendations on small joint injections, see Table 7.

#### **Table 7. Statements and Recommendations on Small Joint Injections**

#### **Statements**

1. US guidance is superior to landmark based guidance when performing small joint injections. *Level of certainty: High* 

2. The use of IACS in the treatment of *osteoarthritis* of *the carpometacarpal joints* of the hands and wrists does not result in short- or long-term improvement in pain or function. IACS results in less pain with movement in patients with *interphalangeal joints of the hand*. *Level of certainty: Moderate* 

3. The use of IACS in the treatment of *rheumatoid arthritis* of the joints of the hands of wrists results in short (12 weeks) or long (12 months) term improvement in pain, function, and inflammation. *Level of certainty: High* 

4. Trigger finger CSI confers a short to intermediate term (3 to 6 months) benefit in resolving symptoms.

*Level of certainty: Moderate* 

5. Triameinolone, 20 mg, is superior to 5 mg and 10 mg for trigger finger injections. *Level of certainty: Low* 

6. DeQuervain's tenosynovitis improves with corticosteroid injections in the short term, and the addition of a thumb splint to the steroid injection leads to intermediate term improvement.

Level of certainty: Moderate

7. Plantar fascia injections with corticosteroids are not superior to placebo injections in *noninflammatory* plantar heel pain.

Level of certainty: Moderate

8. In rheumatic *inflammatory diseases* such as spondyloarthritis, plantar fascia injections with <u>corticosteroids</u> are beneficial in the treatment of pain and inflammation.

*Level of certainty: Low* 

Recommendations

1. Clinicians should preferably offer US guidance when performing injections into the small joints of the wrists, hands, feet, and ankles, as it may provide benefit (e.g., reduced procedural pain) over landmark-based guidance.

Grade C

2. In patients with active *rheumatoid arthritis* in the small joints of the wrists, hands, intra articular corticosteroid injections may be used as an adjunct therapy to decrease pain, improve function, and reduce signs and symptoms of inflammation.

Grade C

3. Clinicians should perform corticosteroid injections for *trigger finger* with 20 mg triamcinolone/methylprednisolone corticosteroid equivalent rather than 5 or 10 mg. *Grade C* 

# 4. Clinicians should offer thumb splints in conjunction with corticosteroid injections for DeQuervain's tenosynovitis.

5. Clinicians may perform plantar fascia injections with corticosteroids for *rheumatic inflammatory heel pain* not responsive to conservative measures.

6. Avoid plantar fascia injections with corticosteroids for *non-inflammatory plantar heel pain*. Grade D

Similar to corticosteroid joint injections, clinicians should limit the use of IACS injections into the small joints of the wrist, hand, and foot. Repeat injections should be based on the patient's response.

#### Safety, adverse events, and monitoring

IACS and other CS injections provides symptomatic relief for patients with a relatively low risk of adverse effects.<sup>214-216</sup> As with other injections, risks include risk of superficial bleeding or hemarthrosis, and temporary worsening of pain. Specific to joints, joint swelling, superficial or joint infection, temporary facial flush, lipoatrophy, or pigment loss around the injection site, interphalangeal calcification and acute post-injection inflammatory arthritis may occur.<sup>122,217-226</sup> Systemic effects from CSI may include hyperglycemia, decreased bone marrow density, and adrenal suppression (though no cases of clinical adrenal insufficiency have been described).

#### **Bleeding**

In a retrospective study of 514 patients on therapeutic anticoagulation with warfarin who underwent a total of 640 joint injections and/or arthrocentesis found a single incident of clinically significant bleeding in an anticoagulated patient (international normalization ratio, [INR] 2.3) (rate of 0.2%).<sup>227</sup> A total of 456 procedures were performed when INR was greater than 2.0, and 184 procedures were performed with INR < 2.0. Another single center retrospective

study of adult patients on novel oral anticoagulants found no incidents of bleeding among 1050 consecutive procedures, with the authors concluding that holding oral anticoagulation prior to joint injections is not warranted.<sup>228</sup>

The American Society of Regional Anesthesia and Pain Medicine recommends that patients on anticoagulant and antiplatelet medications without additional complicating coagulopathic conditions (advanced liver disease or cirrhosis, advanced renal disease, old age, history of bleeding/hemophilia, or multiple anticoagulant medications) may continue their anticoagulant or antiplatelet treatments without interruption for low bleeding risk procedures (such as peripheral joint injection) as the risk for stopping these medications likely outweighs the low risk of bleeding for those on therapeutic dose.<sup>229</sup> Indeed, even patients with knee pain due to hemophilic arthropathy have been shown to derive benefit from IACS, and knee injections have been shown to be performed safely in this population with use of US and Power Doppler.<sup>230</sup>

#### **Cartilage, Ligament and Tendon Health**

One of the concerns with IACS for the knee is the potential adverse effect of IACS on cartilage health. Potential detrimental effects include catabolic effects on cartilage proteins including aggrecan, type II collagen, and proteoglycans, chondrocyte availability, and gross cartilage morphology<sup>231-234</sup> Animal studies investigated the effects of corticosteroid on cartilage with inconsistent and conflicting results.<sup>231,232,235-237</sup> Some of these studies demonstrated cartilage disruption while others showed cartilage preservation during acute inflammatory events. For commonly employed corticosteroid preparations, such as methylprednisolone, betamethasone, and triamcinolone, basic science and animal studies have demonstrated a dosedependent detrimental effect of on cartilage.

A 2-year randomized placebo-controlled, double-blind trial of IA TA vs. saline for symptomatic knee arthritis in 140 patients utilizing annual knee MRIs, IACS resulted in greater cartilage volume loss than saline injection.<sup>238</sup> In this study, the intervention (saline or 40 mg triamcinolone without IA local anesthetic administration) were administered every 12 weeks for 2 years. Patients received MRIs at 0 (baseline), 12, and 24 months, and mean cartilage thickness was computed. Not only was cartilage loss more significant with the corticosteroid, but a corresponding response with pain improvements also did not occur raising concern about the value of frequent repeat IACS for the knee.

As noted previously, cases of tendon rupture were reported after injection into the biceps tendon or into the iliotibial band. <sup>93,94,168</sup> The long-term risks of repeated injections of the tendon sheath have not been reported, but in vitro studies indicated damage to chondrocyte viability after exposure to methylprednisolone.<sup>239</sup> Single doses of ultrasound-guided injections of the biceps tendon do not appear to cause changes in tendon elasticity.<sup>240</sup> Practitioners may choose to exercise caution in performing repeated corticosteroid injections of the biceps tendon or iliotibial band.

#### Accelerated joint space narrowing and osteonecrosis

A IACS knee RCT study (40 mg IA TA injections administered every 3 months vs. saline placebo for up to two years) used x-rays (rather than MRI) to examine radiological progression of joint space narrowing.<sup>241</sup> The study was powered (34 patients per group) to detect a difference of 0.125 mm progression of joint space narrowing between the two treatment groups at 2 years. No difference between the groups were detected at either 1- or 2-year follow up.

A study utilized radiographic findings to assess progression of joint space narrowing or joint destruction (semi-quantitative 0-4 scale) in 30 individuals with OA and 35 with RA that

underwent a minimum of 15 knee corticosteroid injections over a 4-year period and a maximum of 167 injections over a 12-year period.<sup>242</sup> Fifty percent (36) knees showed no or minimal progression between radiographs (duration not described). Ten knees showed marked deterioration (marked narrowing with some collapse of a condyle and/or lateral subluxation). Two knees (same patient) revealed gross deterioration (Charcot's type joint), over 7 years after 82 and 85 IACS provided for each knee. However, there was no correlation between the number of injections and rating of joint deterioration. Again, follow up radiographs were done for elinical indications (not by protocol) with variable follow up (not described). The total number of injections rather than frequency per year were described; laterality was not addressed. The authors concluded that repeated IACS do not lead to rapid joint destruction.

An updated Cochrane Review of IACS for knee OA found that corticosteroid had no effect on joint space narrowing compared to control interventions (standard deviation -0.02; 95% CI, -0.49 to 0.46).<sup>243</sup>

Two retrospective studies showed progression of OA with IACS (based on Kellgren-Lawrence radiographic grading of OA) compared to non-injected controls. One is a small retrospective study with hip OA,<sup>244</sup> the other is a bigger multi-institutional study of 684 patients with knee OA.<sup>245</sup> The retrospective study of 70 patients with hip OA compared to a matched control group showed that 44% (31 of 70) of patients who were given injections of corticosteroids with local anesthetics had radiographic progression of their OA, and 17% (12 of 70) experienced collapse of the articular surface.<sup>244</sup> The two radiologists, blinded to receipt of hip injection, found osteonecrosis in 8-9 images prior to injection and new osteonecrosis in 16-19 images post-injection. There was a very high prevalence of x-ray defined osteonecrosis in both the IACS group (37%) and comparator group (24%).<sup>244</sup> The larger multicenter longitudinal

observational study followed 684 propensity score matched participants. Using either an increase in the Kellgren and Lawrence grade by >1 grade or a decrease in joint space by >0.7 mm for knee rapid OA progression, the authors noted an association between IACS and knee radiographic OA progression.

Finally, there is also a case report of collapse of the superior femoral head articular surface after IACS administration in a patient with osteonecrosis but with preserved femoral head contours.<sup>122</sup> This progression has to be kept in mind since patients with painful noncollapsed osteonecrosis of the femoral head are frequently referred for IACS. The case also demonstrates value in radiographic imaging before IACS hip injections.

The risk factors for osteonecrosis include a history of BMD compromise; chronic corticosteroid exposure; and underlying disorders, such as renal insufficiency, organ transplantation, graft versus host disease, inflammatory bowel disease, HIV, and acute lymphoblastic leukemia.<sup>122,246</sup> Bisphosphonate therapy may mitigate this risk.<sup>247</sup>

#### **Accelerated OA progression**

Rapid progressive OA (RPOA), also called rapid destructive hip disease, or rapid destructive OA, is a rare condition with rapid loss of joint space on x-rays that is beyond the anticipated rate; defined as a joint space loss of more than 2 mm within a 12-month period.<sup>122</sup>

A report of 307 patients undergoing hip IACS noted 23 patients (7%) developed RPOA and of the 152 patients undergoing knee IACS, 6 (4%) were observed to experience RPOA.<sup>122</sup> This study was limited by retrospective review of the clinical care. Radiographic follow up was incomplete, obtained only when clinically indicated, and this would result in conservative estimates. Selection bias (referral to radiology department for image-guided injections) may have been selected for patients with more progressive osteoarthritis (independent of IACS).

A recent two-part study documented an association between hip corticosteroid injection and RPOA.<sup>248</sup> In the case-control portion, the authors showed an association between corticosteroid injection and RPOA, with the risk increased with higher dosage and number of injections. The risk was low with a single 40 mg triamcinolone injection and higher with higher does (80 mg or higher) and multiple (2 or more) injections. (The minimum effective dose is 40 mg TA (see table 8). In the retrospective portion, the investigators noted a rate of 5.4% (37 of 688 cases) after injection. Diagnosis occurred at an average of 5 months after injection and characterized by rapid narrowing of the joint space, osteolysis and collapse of the femoral head.

#### Systemic effects of CS injections

#### **Blood Glucose**

IA corticosteroid is known to elevate blood glucose in patients with and without diabetes mellitus, although not necessarily with adverse clinical consequence in patients without diabetes. Shoulder IACS (triamcinolone 40 mg) for the treatment of ACs elevated fasting blood glucose (FBG) by 17 mg/dL in both diabetic and non-diabetic patients resulting in higher levels at day 1 (attributable to higher baseline FBG); FBG was observed to remain above baseline up to 2 weeks following injections for both groups.<sup>249</sup> Among 60 patients with diabetes mellitus who received IACS, fasting and postprandial blood glucose was observed to be elevated up to 3 days after injection among the entire cohort.<sup>250</sup> However, when analyzed according to site, upper extremity injections were not found to be associated with increased fasting or postprandial blood glucose, knee injections were associated with significantly elevated fasting and postprandial blood glucose, or postprandial blood glucose on days 1 through 7. In multivariate analyses, high baseline glycosylated hemoglobin (HbA1c) was significantly associated with elevated blood glucose

following IACS, while factors including body mass index, insulin use, and corticosteroid dose were not associated with elevated blood glucose. In this study, one patient had FBG as high as 493 mg/dL, but no patient experienced diabetic ketoacidosis.<sup>250</sup> A study of 23 diabetic patients undergoing IACS shoulder injection reported similar findings, namely no significant elevation of blood glucose above baseline following injection.<sup>251</sup> One RCT of diabetic patients on oral agents undergoing IA knee CSI compared extended release to standard formulations of triamcinolone (32 mg) vs. standard triamcinolone preparations (40 mg).<sup>31</sup> The mean increase in blood glucose from pre-injection (days 3 to -1) to post injection (days 1 to 3) was 37 mg/dL and significantly greater than the 8.2 mg/dL in the extended release group (P = .04); blood glucose after standard 40 mg triameinolone was noted to peak 6 hours after the injection with mean blood glucose of 252 mg/dL.<sup>31</sup> A systematic review of patients with diabetes mellitus undergoing IACS identified 7 studies (N = 72) showing a clinically significant rise in blood glucose up to one week after injection, with many patients experiencing this effect within 48 to 72 hours after injection but not necessarily immediately following the procedure.<sup>252</sup> In a study evaluating the effects of TH vs. TA on blood glucose following IACS in patients with diabetes and symptomatic knee OA (N = 12 in each cohort, and N = 6 in a hyaluronic acid cohort), patients experienced median elevated blood glucose >200 mg/dL following IASC, (median peak 239.5 at 32.5 hours in the TH group, 288 at 24.5 hours in the TA group) returning to normal within approximately 4 days.<sup>253</sup> All study subjects had HbA1c <7.0. A separate small study following 6 patients with controlled diabetes after IACS with betamethasone to the knee joint showed a mean peak blood glucose of 322.5 + 67.75 mg/dL, with most patients returning to baseline with 48 hours following injection.<sup>254</sup>

#### **Bone mineral density**

Chronic and/or high-dose corticosteroid exposure is known to affect bone mineral density (BMD), particularly in patients with conditions requiring long-term oral medication. Excessive use of epidural corticosteroid injections has been associated with compromised BMD.<sup>255-258</sup> Kerezoudis et al noted significant reductions in BMD were associated with a cumulative dose of 200 mg over a one-year period and 400 mg over 3 years, and at least 3 grams for healthy men. Reductions in BMD were not seen in doses of less than 200 mg of MP equivalents for postmenopausal women.<sup>255</sup> Their conclusions were questioned in view of the small and underpowered studies that they reviewed.<sup>256</sup> In a subsequent narrative review of additional studies, Stout et al recommended consideration of a maximum cumulative whole body triamcinolone/ methylprednisolone dose of 200 mg per year and 400 mg per 3 years in postmenopausal women and potentially men over age 50.<sup>258</sup> They cautioned that these relative limits should be weighed against functional benefits. Additionally, another study of 352 postmenopausal women concluded that there was no association between epidural corticosteroid injections and decreased BMD or fracture risk.<sup>257</sup> These studies are discussed in more detail in our upcoming neuraxial steroid practice guideline.

Regarding IACS, a retrospective study in patients with rheumatoid arthritis (N = 208 patients, receiving 1 [101 patients], 2-3 [51 patients]or 4 [56 patients] IACS did not find any statistically significant relationship between number of IACS and BMD over the course of one year.<sup>259</sup>

A recent cohort study by Sytsma et al was published after we developed the SRs.<sup>260</sup> This study is notable for the large number of injections and the variety of corticosteroid injections. The investigators evaluated the association between the risk of fracture and 33, 864 CSIs into

joints (large, medium, small), spine (facet, epidural, sacroiliac), nerve blocks, trigger points, and tendon or ligament. They did not see an association between higher fracture risk based on cumulative corticosteroid dose, with a mean cumulative dose of 141.8 mg TA equivalents (range: 2.7-2140.3 mg). Sytsma et al also noted the lack of associated higher fracture risk in the non-high-risk or osteoporosis subgroups.<sup>260</sup> This supports the findings of Kerezoudis study in which BMD was not decreased at doses of less than 200 mg of MPA/TA equivalents per year for postmenopausal women.

The recommendations of Kerezoudis et al and Stout et al were made after a careful review of the literature. Balancing the recommendations of Kerezoudis et al and Stout et al with the results of the recent study by Sytsma et al, we *suggest* that the clinician *consider* a maximum cumulative whole body triancinolone dose equivalent of 200 mg per year and 400 mg per 3 years in postmenopausal women. Note that the average and maximum TA equivalent cumulative dose was higher in the Kerezoudis et al study (average of 80 to 81309 mg in the eight studies) compared to the Sytsma et al study (2140.3 mg) We arrived at this suggestion to err on the side of safety, as we wait for additional studies. These limits are achievable without compromising efficacy. Routine series of injections should not be performed; subsequent injections should be repeated after observation of the patient's response and after recurrence of the pain. The minimum effective doses of corticosteroid injections in the joints and in the spine should be administered; CS should not be added in sympathetic nerve blocks, TPIs and most peripheral nerve blocks. We echo the recommendation by Stout et al that providers should discuss the potential of BMD loss after glucocorticoid injections with patients, especially when receiving multiple injections.

# **Adrenal suppression**

Adrenal suppression has been documented after single IA doses of corticosteroids.<sup>261-263</sup> Clinically meaningful adrenal insufficiency occurs when a sufficient stress requires an adrenal surge in the setting of adrenal suppression; it is an uncommon but important clinical condition that may occur more commonly or be expected in the hospital setting.

An RCT compared patients who received a single knee IACS (MPA 80 mg) with a group that received 6 mL IA sodium hyaluronate. This was followed by a low-dose adrenocorticotropic hormone (ACTH) stimulation test. The authors noted that 25% of subjects in the steroid group experienced secondary adrenal insufficiency (<7 microgram/dL increase in serum cortisol level and absolute levels of <18 microgram/dL 30 minutes after the ACTH stimulation test), observed 2-4 weeks following injection vs. none in the control group.<sup>264</sup> A systematic review and metaanalysis noted that the percentages of adrenal insufficiency ranged from 4% with intranasal administration to 52% from IA injection.<sup>265</sup>

### Septic Arthritis

The incidence of septic arthritis following IACS outside of the context of joint replacement surgery is rare, but patient morbidity can be devastating.

Risk factors for septic arthritis include immunosuppression, intravenous drug use, alcoholism, previous steroid injections, and cutaneous ulcers. Patients commonly present with local warmth and/or swelling, fever, and night pain, and the most involved joints include the knee and hip.

A retrospective review of 10 patients diagnosed with acute septic arthritis following knee injection found that 3 out of 10 patients had undergone recent injection with "cortisone" (5 with hyaluronic acid, 2 unknown).<sup>266</sup> All patients presented with joint pain and swelling; 3 had decreased ROM, 2 had fever, and 1 had erythema. The mean incubation period was 11.9 days.

Inflammatory markers were elevated (mean erythrocyte sedimentation rate [ESR], 52.6 mm/h; mean C-reactive protein [CRP], 10.3 mg/dL). Only half of the 10 patients had an organism identified in culture (3 *Streptococcus mitis*, 2 oral flora). Comorbidities included hypertension (4 patients), diabetes mellitus (2), and chronic kidney disease (1). Patients had received a variable number of injections prior to admission (0-1 in 4 patients, 2-3 in 4, 4-5 in 2). All 10 patients underwent arthrocentesis with cell culture and were treated surgically (3 patients required more than one incision and drainage). Of the patients, 8 were treated with antibiotics for 21 days (7 with parenteral antibiotics), and 6 were dismissed to a rehabilitation facility. With a broader assessment of risk factors associated with these infections, the authors concluded that the facility performing the injections had poor adherence to standard infection control protocols.

Sterile inflammatory arthritis may occur after IA injection and can be confused with septic arthritis. A systematic review identified 19 patients among 18 studies (N = 286) with post-injection swelling without clinical evidence for infection consistent with synovitis.<sup>267-269</sup> Post-injection inflammation may be due to exacerbation of calcium pyrophosphate dihydrate crystals, which has been best described after sodium hyaluronate injection.<sup>270</sup>

### Safety of IACS prior to joint replacement surgery

IACS in the pre-operative joint replacement setting raises concern for prosthetic joint infection (PJI). Guidance from professional societies and federal agencies is vague. The AAOS states that there is limited evidence to suggest that IA injections may have a time dependent association for increased risk of PJI and that the overall event rate is low.<sup>13</sup> The US Centers for Disease Control and Prevention (CDC) cited low quality evidence precluding recommendations about preoperative IACS.<sup>271</sup> The 2017 American College of Rheumatology (ACR)/American Association of Hip and Knee surgeons (AAHKS) Guideline for Perioperative Management did

not include comments or recommendations about the timing of preoperative IACS.<sup>272</sup>–In a survey of AAHKS members, 93% cited that a 3-month interval should be the minimum interval between IACS and joint replacement surgery.<sup>34</sup>

Literature review and manual search resulted in articles that fell into 3 principal methodologies: 1) small single-institution cohorts, 2) administrative data reviews, and 3) systematic literature reviews.

#### Large administrative database analyses knee

Given the infrequent outcome of PJI, the majority of the patient-derived data came from analyses of large administrative datasets. All knee analyses<sup>273,276</sup> were derived from the PearlDiver National Insurance Claim Database, which captures data from Humana, United Healthcare, and Medicare.<sup>277</sup> There are variations in 1) the dates of patients sampled, 2) the granularity of the pre-operative IACS window, 3) the definition of infection (superficial vs. deep) and 4) post-operative follow up (6 vs. 12 months) across the studies. A single study evaluated the difference between CSI vs. hyaluronate injection.<sup>274</sup> Three large administrative analyses reported statistically significant increases in PJI risk when total knee arthroplasty (TKR) closely followed an IACS. Infection risk in the comparator group without preceding injection ranged from 1% to 2.7% depending partly on length of post TKR observation. All studies reported statistically significant increased multivariate odds or hazard ratio for the time periods closest to surgery. Bedard et al reported an increased risk for pre-operative injections done in a 6-month window preceding TKR; however, there was no detectable increased risk when injections were performed after 6 months.<sup>275</sup> By contrast, Cancienne and colleagues noted an increased incidence of infection when steroid was injected within 3 months, with no increased risk when the surgery was done 3 months after injection.<sup>276</sup> In a study of 76,090 patients, Bhattacharjee et al found that

the 0–2-week window for IACS had a significantly increased risk of infection with a trend for increased risk when injections were performed within 2–4 weeks of surgery.<sup>273</sup> The 4-week interval was reinforced in a later study by Bains et al.<sup>278</sup> They analyzed 9,766 patients (4766 had IACS, 5000 without injection) and noted significant risk of surgical site of infection when the IACS was done within 4 weeks prior to the TKA. There was no infection risk when the interval was beyond 4 weeks.

For the studies with multivariate analyses,<sup>273,274,276</sup> the presence of diabetes, obesity, inflammatory arthritis, or RA all carried significant risk of PJI (regardless of pre-operative IA injection).

#### Large administrative database analyses hip

-Two separate large administrative analyses that focused on the risk of infection after total hip replacement (THR).<sup>279,280</sup> Both studies found that the IACS within the 3-months of THR resulted in higher rates of PJI. Both studies noted no increased infection risk for IACS given between 3 and 6 months or between 6 and 12 months.<sup>279,280</sup>

Three systematic literature reviews were identified (1 hip from 2016, 1 knee from 2014, and 1 hip or knee from 2014). Charalambous and colleagues concluded that pre-operative IACS was not associated with increased risk PJI after THR or TKR, citing a non-significant trend for increased risk and lack of a clear mechanism of action for delayed PJI.<sup>281</sup> Marsland and colleagues evaluated four level 3 evidence studies and reported concern about observed trends but described the data as insufficient to provide recommendations beyond awareness of the risk and optimization of known infection risk reduction peri-operative strategies.<sup>282</sup> Pereira analyzed 8 retrospective studies and a single observational cohort (N = 49) and found the level of evidence insufficient to provide recommendation.

and data analyzed. A 2023 review and meta-analysis evaluated 11 retrospective matched-cohort or case-control studies and concluded that the risk of infection is increased when an IACS is performed within 3 months of THR.<sup>284</sup>

### Intraoperative IA steroid injection knee and hip

One systematic review identified a total of 12 studies (N = 863) comparing safety and efficacy of IACS given intraoperatively during TKR/THR.<sup>285</sup> Results indicated that patients experienced superior analgesia and less post-operative nausea and vomiting in the immediate post-operative period with no difference in adverse effects compared to injection with saline. The authors speculated that the safety of intraoperative IACS may be due to the sterile environment of the operating room and careful post-operative monitoring.<sup>285</sup> Another study, however, showed an increased rate of infection after intraoperative ICAS in patients who had ankle arthroscopy.<sup>286</sup> The authors noted most infections occurred in the 65-79 age group.

### **Comments on preoperative IACS and PJI**

The literature evaluating PJI after pre-operative IACS is based on administrative databases, underpowered observational cohorts, variability in definition of PJI, and duration of follow-up. Providing IACS during the 3-month pre-operative period <u>may carry</u> increased risk of PJI, especially if done within 2-4 weeks of TKR.<sup>273,278,284</sup>

For Statements and Recommendations on adverse events see Table 8.

# Table 8. Statements and Recommendations on Adverse Events from IntraarticularCorticosteroid Injections

Statements
1. Clinically significant increases in blood glucose may follow intra articular corticosteroid (IACS)
injection, particularly in patients with diabetes mellitus. These effects are noted within hours of IACS,
but peak blood glucose may be delayed for up to 2 days after IACS.
Level of certainty: High
2. Extended-release corticosteroid preparations may mitigate the impact of IACS on systemic blood
glucose in patients with diabetes.
Level of certainty: Moderate
3. Adrenal suppression may follow an intra articular corticosteroid injection.
Level of certainty: Moderate
4. For warfarin, in patients with an INR in the therapeutic range (2.0 3.0), the risks of withholding
anticoagulation prior to IACS related to development of a thromboembolic event are greater than the
risks of bleeding
Level of certainty: Low
5. When there is strict adherence to standard infection control practices, the risk of infection due to
IACS is low.
Level of certainty: Moderate
6. There is an increased risk of post-operative deep joint infection when IACS is administered within 3
months prior to that joint replacement surgery, especially if IACS is performed within 1 month of
surgery.
Level of certainty: Moderate
7. There is a trend towards increased risk of postoperative deep joint infection when IACS is
administered within 3 months prior to that joint replacement surgery.
Level of certainty: Low
Recommendations
1. Patients with diabetes mellitus should be advised to monitor blood glucose carefully post injection
for at least 48 hours, until blood glucose normalizes (possibly up to 7 days).
Grade A
2. Monitoring of cortisol levels pre-or post IACS is not recommended routinely.
Grade D
3. In the right clinical setting, adrenal crisis should be considered as possible etiology in the
hypotensive patient in the days or weeks following IACS.
Level of certainty: Low
4. For patients on chronic stable warfarin therapy with good control (no bleeding symptoms),
anticoagulation therapy need not be withheld for IACS; patients on warfarin may be in therapeutic INR
Fange.
Grade A
5. Providers should adhere to standard infection control practices including strict aseptic technique
when performing IACS.
Grade A
6. Avoid IACS within 3 months of planned total replacement of that joint, notably within 1 month
of planned surgery.
Grade D
7. Discuss with the surgeon the risks/benefits when considering IACS in a joint planned for
replacement surgery within 3 months.
Grade C

Limitations and timeline of this PG

Limitations of our guideline include non-inclusion of stakeholders, e.g., patient advocacy

groups) and incomplete adherence to the AGREE II recommendations,<sup>287,288</sup> similar to other

guidelines.<sup>289</sup> This PG will be updated in five years, when adequate controlled trials and

systematic reviews and meta-analyses are published necessitating revision of our

recommendations.

Table 9. Minimum Effective and Commonly Used Doses of Intraarticular, Bursa, and TendonCorticosteroid Injections

Controsteroita injection		1	
Study	Joint/Bursa/Tendon	Steroid, Dose	Indication
Minimum effective			
dose (based on dose-			
<del>response studies)</del>			
Onks et al <sup>81</sup>	IACS, glenohumeral	Triamcinolone	Glenohumeral
<del>Yoon et al<sup>82</sup></del>	joint	acetonide, 20mg	arthritis; adhesive
Kim et al <sup>83</sup>	•		capsulitis
Hong et al <sup>84</sup>	SASDB	Triamcinolone	Rotator cuff tear
Ŭ		acetonide, 20mg	
Carroll et al <sup>85</sup>	SASDB	Triamcinolone	Shoulder pain
		acetonide, 20mg;	1
		MPA 20 mg	
Popma et al <sup>173</sup>	Knee joint	TA, 40 mg	Knee osteoarthritis
r opina or ar	Timee Joint	ini, to ing	
Kosiyatrakul et al <sup>203</sup>	Trigger finger	<del>TA, 20 mg</del>	Trigger finger
Rosiyatiakui et ai	inger inger	17 <b>1</b> , 20 mg	mgger mger
Commonly used			
doses			
Hanson et al <sup>32</sup>	Long head of biceps	TA, 40 mg	Tendinitis of the long
Zhang et al <sup>89</sup>	<b>U</b> 1	TA, 20 mg in diabetic	head of the biceps
Yiannakopoulos et		patients	1
al <sup>90</sup>		1	
Qian et al <sup>101</sup>	Lateral epicondyle	TA, 20, 40, 80 mg	Lateral epicondylosis
Krogh et al <sup>102</sup>	1 5	MPA, 20, 40 mg	1 ,
Bisset et al <sup>103</sup>		Betamethasone, 6 mg	
Coombes et al <sup>104</sup>		Dexamethasone, 4	
Gaujoux-Viala et al <sup>105</sup>		mg	
Assendelft et al <sup>106</sup>			
Bisset et al <sup>107</sup>			
Stahl et al <sup>113</sup>	Medial epicondyle	<del>MP, 40 mg</del>	Medial epicondylosis
Kim et al <sup>116</sup>	Olecranon bursa	<del>TA, 40 mg</del>	<del>Olecranon bursitis</del>

Lambert et al <sup>123</sup>	Hip joint	<del>TH, 40 mg</del>	Hip joint
<del>Park et al<sup>127</sup></del>	1 5	<del>TA, 40 mg</del>	osteoarthritis
Jurgensmeier et al <sup>128</sup>		MPA, 40 mg	
<del>Ovistgaard et al<sup>129</sup></del>			
Atchia et al <sup>130</sup>			
Young et al <sup>135</sup>			
Migliorini et al <sup>136</sup>	Greater trochanteric	MPA, 40 mg	Greater trochanteric
Brinks et al <sup>158</sup>	<del>bursa</del>	<del>TA, 40 mg</del>	<del>bursitis</del>
Rompe et al <sup>159</sup>		<del>TH, 80 mg</del>	
Nissen et al <sup>160</sup>		Prednisolone, 25 mg	
		Betamethasone, 1 mL	
		<del>(5 mg/mL</del>	
		betamethasone	
		dipropionate and 2	
		mg/mL	
		betamethasone	
		sodium phosphate	
Mellor et al <sup>165</sup>	Gluteus	TA, 40 mg	Gluteus
Mellor et al	medius/minimus	Betamethasone, 5.7	medius/minimus
	tendon	<del>mg (1 mL)</del>	tendinopathy
Wang et al <sup>187</sup>	Wrist joint	<del>TA, 40 mg</del>	Arthritis of joint
<del>Kroon et al<sup>196</sup></del>			
Nam et al <sup>201</sup>	Distal radioulnar joint	<del>TA, 20 mg</del>	Arthritis of joint
Wang et al <sup>187</sup>	<b>Metacarpophalangeal</b>	<del>TA, 20 mg</del>	Arthritis of joint
	joint		
Wang et al <sup>187</sup>	Interphalangeal joint	<del>TA, 20 mg</del>	Arthritis of joint
Kroon et al <sup>196</sup>		<del>TH, 4-6 mg</del>	
Kroon et al <sup>196</sup>	Carpometacarpal	TA, 10 mg, 20 mg, 40	Arthritis of joint
<del>Meenagh et al<sup>198</sup></del>	<del>joint</del>	mg	
		Betamethasone, 6 mg	
		<del>(1 mL), 3 mg (0.5</del>	
		<del>mL)</del>	
		<del>TH, 5 mg</del>	
Huisstede et al <sup>204</sup>	Tendon, thumb side	<del>TA, 10 mg, 20 mg</del>	DeQuervain (radial
	<del>of wrist</del>	<del>МРА, 40 mg</del>	styloid) tenosynovitis
		Betamethasone, 6 mg	
		<del>(1 mL)</del>	
207			
David et al <sup>206</sup>	Plantar fascia	<del>TA, 20, 40, 80 mg*</del>	Plantar fasciitis
Whittaker et al <sup>207</sup>		MPA, 20, 40, 80 mg	
Hansen et al <sup>209</sup>		Betamethasone, 6 mg	
Babatunde et al <sup>210</sup>		Dexamethasone, 4, 8	
Abdelghani et al <sup>211</sup> *Plantar fasciitis TA a	nd MPA · No dose respon	mg nse studies but 20 mg do	

Plantar fasciitis, TA and MPA: No dose-response studies but 20 mg dose shown to be effective.

#### **Summary**

IACS and soft tissue musculoskeletal injections are employed in the management of joint pain related to arthritis, most commonly for OA and tendinosis/tendinitis and bursitis. Injections are usually performed when non-pharmacological treatment and systemic analgesics fail to provide relief of the symptoms. Our PG is the result of an extensive review of the literature and rigorous modified Delphi process.

The exact etiology of pain in the shoulder and in the hip should be identified, using the patient's history, physical examination including provocative tests, and the results of diagnostic studies including imaging. This is critical to proper treatment, including whether injection therapy is appropriate and the correct target for injection.

Image guidance, fluoroscopy or US, increases the accuracy of injections although longterm outcomes (pain and function) did not show a difference. Some studies showed improved accuracy of US compared to fluoroscopy in some injections (biceps tendon injection), while others did not (hip joint, glenohumeral joint). Ultrasound requires less equipment; there is no associated radiation; and patients appear to prefer it over fluoroscopy. Ultrasound requires expertise; hence the physician should employ imaging modality with which they are most experienced and comfortable.

There is little evidence to guide the selection of one corticosteroid over another. A dose of 20 mg triamcinolone is as effective as 40 mg TA for shoulder IACS. The most commonly used dose for hip IACS was 40 mg TA or MPA. Triamcinolone 40 mg is as effective as 80 mg for knee IACS. The commonly used corticosteroid doses are noted in **table 9**. We suggest a *minimum interval* of 2-3 weeks between injections, up to three months. The series of injections can be stopped when there is complete or acceptable pain relief or when the relief has plateaued,

taking into consideration the maximum cumulative dose. Overall, IACS results in short-term (4 weeks to 3 months) pain relief.

The AEs from IACS are related to the procedure as well as to local and systemic effects of the corticosteroid. These include increase in blood glucose, adrenal suppression, detrimental effect on cartilage, reduction of bone mineral density, and PJI. Identification of the patient at risk, injection of minimum effective doses, proper monitoring, timing of injection in relation to planned total joint surgery should eliminate or mitigate most of these AEs. Adherence to the recommendations in this practice guideline is a foremost step in the proper care of patients who need IACS, bursa, and tendon injections.

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### Legends

Figure 1. Injections sites for shoulder pain. A aeromioelavicular joint; B subacromial subdeltoid bursa; C long head of the biceps tendon; D glenohumeral joint. Note that the injection is around the biceps tendon or tendon sheath. Image courtesy of Sebastian Encalada, MD, Mayo Clinic, Jacksonville, Florida.

Figure 2: Injections sites for hip pain. A iliopsoas bursa; B gluteus medius/minimus tendon sheath; C greater trochanter bursa; D hip joint. Note that the injection is around the gluteus medius/minimus tendon or tendon sheath. Image courtesy of Sebastian Encalada, MD, Mayo Clinic, Jacksonville, Florida.

# **Tables**

Table 2. Modified United States Preventive Services Task Force (USPSTF) Grades and Suggestions for Practice

Table 2. Modified United States Preventive Services Task Force (USPSTF) Levels of Certainty Regarding Net Benefit

Table 3. Statements and Recommendations on Steroid Pharmacology

<u>Table 4.</u> Statements and Recommendations on Interval Between Injections and Role of Imaging in Intraarticular Corticosteroid Injections

<u>Table 5.</u> Statements and Recommendations on Intraarticular Corticosteroid Injections in Shoulder and Elbow

<u>Table 6.</u> Statements and Recommendations on Intraarticular Corticosteroid Injections in Hip and Knee Joints

Table 7. Statements and Recommendations on Small Joint Injections

<u>Table 8.</u> Statements and Recommendations on Adverse Events from Intraarticular Corticosteroid Injections

<u>Table 9.</u> Minimum Effective and Commonly Used Doses of Intraarticular, Bursa, and Tendon Corticosteroid Injections

#### Boxes

Box 1. Recommendations of National Organizations on Usefulness of Hip and Knee Intraarticular Corticosteroid Injections

Box 2. Absolute and Relative Contraindications to Intraarticular and Soft Tissue Corticosteroid Injections

Box 3. Clinical tests in greater trochanteric pain syndrome

# Supplemental Appendix

Literature Search, with MeSH terms

1. Indications; choice of steroid; comparison of steroids: John FitzGerald, MD, PhD

2. Frequency of injections; annual cumulative dose: Dmitri Souza, MD; John FitzGerald, MD, PhD

3. Role of fluoroscopy and ultrasound: Ameet Nagpal, MD, MS, MEd, MBA; Dmitri Souza, MD; Honorio T. Benzon, MD

4. Shoulder joint injections: Maxim S. Eckmann, MD

5. Shoulder joint injections: Glenohumeral instability; Scapulothoracic articulation disorders; Glenohumeral joint; Tendinitis of the long head of the biceps: Honorio T. Benzon, MD

6. Hip injections: Dmitri Souza, MD

7. Greater trochanteric pain syndrome: Greater trochanteric pain syndrome; Greater trochanteric bursitis; Gluteus medius/minimus tendinopathy; Snapping hip syndrome; Iliotibial band friction syndrome: Honorio T. Benzon, MD

8. Knee injections: David A. Provenzano, MD

9. Small joints: Ameet Nagpal, MD, MS, MEd, MBA

10. Postinjection protocols: Ameet Nagpal, MD, MS, MEd, MBA

11. Safety, adverse events, monitoring: Christine L. Hunt, DO; John FitzGerald, MD, PhD

12. Pharmacokinetics of joint steroid injections: Honorio T. Benzon, MD

# Interval between steroid injections (frequency of injections) and annual cumulative dose Dmitri Souza, MD

John Fitzgerald, MD

Index Used for Search: PubMed

Search: (steroid) AND (intraarticular) AND (injection) AND (frequency)

("steroidal"[All Fields] OR "steroidals"[All Fields] OR "steroidic"[All Fields] OR "steroids"[MeSH Terms] OR "steroids"[All Fields] OR "steroid"[All Fields]) AND ("injections, intra articular"[MeSH Terms] OR ("injections"[All Fields] AND "intra articular"[All Fields]) OR "intra-articular injections"[All Fields] OR ("intraarticular"[All Fields] AND "injection"[All Fields]) OR "intraarticular injection"[All Fields]) AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "frequency"[All Fields] OR "epidemiology"[MeSH Terms] OR "frequence"[All Fields] OR "frequences"[All Fields] OR "frequencies"[All Fields]) Translations

steroid: "steroidal"[All Fields] OR "steroidals"[All Fields] OR "steroidic"[All Fields] OR "steroids"[MeSH Terms] OR "steroids"[All Fields] OR "steroid"[All Fields]

intraarticular injection: "injections, intra-articular"[MeSH Terms] OR ("injections"[All Fields] AND "intra-articular"[All Fields]) OR "intra-articular injections"[All Fields] OR

("intraarticular"[All Fields] AND "injection"[All Fields]) OR "intraarticular injection"[All Fields]

frequency: "epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "frequency"[All Fields] OR "epidemiology"[MeSH Terms] OR "frequence"[All Fields] OR "frequences"[All Fields] OR "frequences"[All Fields]

Number of Initial Results: 190

Number Included After Screening: 23

# Role of fluoroscopy, ultrasound, and contrast media in minimizing side effects and maximizing outcomes

Ameet Nagpal, MD, MS, MEd, MBA Dmitri Souza, MD

Index Used for Search: PubMed

Search Terms Used: steroids, joint, injections, side effects, imaging

("steroidal"[All Fields] OR "steroidals"[All Fields] OR "steroidic"[All Fields] OR "steroids"[MeSH Terms] OR "steroids"[All Fields] OR "steroid"[All Fields]) AND ("joint s"[All Fields] OR "joints"[MeSH Terms] OR "joints"[All Fields] OR "joint"[All Fields]) AND ("inject"[All Fields] OR "injectability"[All Fields] OR "injectant"[All Fields] OR "injectants"[All Fields] OR "injectate"[All Fields] OR "injectates"[All Fields] OR "injected"[All Fields] OR "injectible"[All Fields] OR "injectates"[All Fields] OR "injecting"[All Fields] OR "injections"[MeSH Terms] OR "injections"[All Fields] OR "injectable"[All Fields] OR "injectables"[All Fields] OR "injections"[All Fields] OR "injectable"[All Fields] OR "injectables"[All Fields] OR "injection"[All Fields] OR "injects"[All Fields]) AND ("adverse effects"[MeSH Subheading] OR ("adverse"[All Fields] AND "effects"[All Fields]) OR "adverse effects"[All Fields] OR ("side"[All Fields] AND "effects"[All Fields]) OR "side effects"[All Fields]) AND ("image"[All Fields] OR "image s"[All Fields] OR "imaged"[All Fields] OR "imager"[All Fields] OR "imager s"[All Fields] OR "imagers"[All Fields] OR "imagers"[All Fields]] Fields] OR "imaging"[All Fields] OR "imaging s"[All Fields] OR "imagings"[All Fields]) Translations

steroid: "steroidal"[All Fields] OR "steroidals"[All Fields] OR "steroidic"[All Fields] OR "steroids"[MeSH Terms] OR "steroids"[All Fields] OR "steroid"[All Fields]

joint: "joint's"[All Fields] OR "joints"[MeSH Terms] OR "joints"[All Fields] OR "joint"[All Fields]

injections: "inject"[All Fields] OR "injectability"[All Fields] OR "injectant"[All Fields] OR "injectants"[All Fields] OR "injectate"[All Fields] OR "injectates"[All Fields] OR "injected"[All Fields] OR "injectible"[All Fields] OR "injectibles"[All Fields] OR "injecting"[All Fields] OR "injections"[MeSH Terms] OR "injections"[All Fields] OR "injectable"[All Fields] OR "injectables"[All Fields] OR "injection"[All Fields] OR "injects"[All Fields]

side effects: "adverse effects"[Subheading] OR ("adverse"[All Fields] AND "effects"[All Fields]) OR "adverse effects"[All Fields] OR ("side"[All Fields] AND "effects"[All Fields]) OR "side effects"[All Fields]

imaging: "image"[All Fields] OR "image's"[All Fields] OR "imaged"[All Fields] OR "imager"[All Fields] OR "imager's"[All Fields] OR "imagers"[All Fields] OR "images"[All Fields] OR "imaging"[All Fields] OR "imaging's"[All Fields] OR "imagings"[All Fields] Number of Initial Results: 153

Number Included After Screening: 21

Additional items from references: 18

# Shoulder Joint Steroid Injection Technique for the Treatment of Acute and Chronic Shoulder Pain

Maxim S. Eckmann, MD Index Used for Search: PubMed Search Terms Used: ((steroids OR Corticosteroids OR Adrenal Cortex Hormones OR Cortisone OR Dexamethasone OR prednisolone OR Glucocorticoids OR methylprednisolone OR betamethasone) AND

(injection OR injectable)) AND ((shoulder or glenohumeral or subacromial or subdeltoid or acromioclavicular or (frozen shoulder)) AND (english[Filter])) NOT (radiofrequency OR surgery OR animal OR knee OR elbow OR hip OR epicondyle OR hand OR botulinum) – Article Types applied: Meta-Analysis, Randomized Controlled Trial, Systematic Review; Additional Filters – 10 years

Number of Initial Results: 63 Number Included After Screening: 34 Additional background references: 2

# Shoulder joint injections: Glenohumeral joint; Tendinitis of the long head of the biceps Honorio T. Benzon, MD

**Glenohumeral instability** PUBMED, MeSH: "Pain from and treatment of glenohumeral instability" Results: 458 articles Used: 4

# Scapulothoracic articulation

PUBMED, MeSH: "Pain from and treatment of scapulothoracic disorders" Results: 115 articles Used: 5

# **Glenohumeral joint**

PUBMED, MeSH: "CSI into the glenohumeral joint" Results: 492 articles PUBMED, MeSH: "CSI into the glenohumeral joint from arthritis" Results: 127 articles Used: 10

# Tendinitis of the long head of the biceps

PUBMED, MeSH: "CSI into the biceps tendon" Results: 53 articles Used: 10

# Steroid Injection for the Treatment of Musculoskeletal Elbow Pain Christine L. Hunt, DO

### **Data Sources and Search Strategies**

A comprehensive search of several databases from each database's inception to August 10th, 2021, any language, was conducted. The databases included Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, and Daily, Ovid EMBASE, Ovid Cochrane Central Register of Controlled Trials, and Ovid Cochrane Database of Systematic Reviews. The search strategy was designed and conducted by an experienced librarian with input from the study's principal investigator. Controlled vocabulary supplemented with keywords was used to search for studies of safety of injected steroids in patient elbows. The actual strategy listing all search terms used and how they are combined is available in the appendix. The review

was then focused to studies published after the year 2000 in order to capture data most relevant to contemporary practice.

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials July 2021, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to August 4, 2021, Embase 1974 to 2021 August 09, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily 1946 to August 09, 2021 Search Strategy:

#	Searches	Results
1	exp Adrenal Cortex Hormones/	1415037
2	exp corticosteroid/	1386716
3	exp corticosteroid therapy/	51008
4	("adrenal cortex hormore" or "adrenal cortex steroid*" or "adrenal cortical hormone*" or "adrenal cortical steroid*" or "adrenal cortical steroid*" or "adrena cortical steroid*" or "adrena cortical steroid*" or "adrena cortical hormone*" or "adreno corticosteroid*" or adrenocortical hormone*" or "adrenocortical steroid*" or adrenocorticosteroid* or adreson or alclometasone or algostone or "algestone acetonide" or amcinonide or amelometasone or ciclopredinol or clopetanol or clobetasol or clopredinsone or ciclogostide or corticosteroid*" or corticosteroid* or corticosteroid*" or corticoid* or corticosteroid* or corticosteroid* or corticoid* or corticosteroid* or dehydrocorticosterone or dehydrocorticosterone or dehydrocorticosterone or diflucrotolone or difluprednate or domoprednate or drocinonide or flucorinsione or flucoronide or flucosteroid* or glucocorticoid* or glucocorticosteroid* or glucocorticosteroid* or glucocorticosteroid* or glucocorticoid* or glucocorticosteroid* or haloretasone or hydroxycorticosteroid* or glucocorticosteroid* or haloretasone or hydroxycorticosteroid* or glucocorticosteroid* or hydroxycorticosteroid* or nor fluorone or fluprednidene or fluprednisolone or flucosteroid* or hydroxycorticosteroid* or glucocorticoid* or glycocorticosteroid* or hydroxy norcorticosteroid* or glucocorticoid* or glycocorticosteroid* or hydroxy norcorticosteroid* or isoflupredone or invocinoide or hydroxy hydrocortisone or invessione or nicrosteroid* or mineralocorticosteroid* or mineralocorticosteroid* or mineralocorticosteroid* or mineralocorticosteroid* or glucocorticosteroid* or glucocorticosteroid* or glucocorticosteroid* or glucocorticosteroid* or glucocorticosteroid* or nydroxy hydrocortisone or invocinole or invocortio or noteoxycorticosteroid* or mineralocorticosteroid* or mineralocorticosteroid* or mineralocorticosteroid* or more hydroxycorticoster	1519577
5	1 or 2 or 3 or 4	2139085
6	exp injection/	481890

7 (injectable* or injection*).ti,ab,kw.	1510023
8 6 or 7	1715788
9 5 and 8	128358
10 exp Elbow/ or exp Elbow Joint/	40666
11 exp Elbow Tendinopathy/	5750
12 exp Arthroplasty, Replacement, Elbow/	555
13 elbow.ti,ab,kw.	80294
14 10 or 11 or 12 or 13	93460
15 9 and 14	1807
16 (safe or safety).ti,ab,kw.	2489594
17 15 and 16	197

("consensus development" or "consensus statement" or "expert consensus" or "consensus document" or "consensus recommendation\*" or "consensus report" or "Delphi consensus" or "consensus study" or "consensus workshop report" or (meta adj analys\*) or metaanalys\* or (systematic\* adj3 review\*) or guideline\* or (control\* adj3 study) or (control\* adj3 trial) or (randomized adj3 study) or (randomized adj3 trial) or (randomised adj3 study) or (randomised adj3 trial) or "pragmatic clinical trial" or (random\* adj1 allocat\*) or (doubl\* adj blind\*) or (doubl\* adj mask\*) or (singl\* adj blind\*) or (singl\* adj mask\*) or (tripl\* adj blind\*) or (tripl\* adj mask\*) or (trebl\* adj blind\*) or (trebl\* adj mask\*) or "latin square" or placebo\* or nocebo\* or multivariate or "comparative study" or "comparative survey" or "comparative analysis" or (intervention\* adj2 study) or (intervention\* adj2 trial) or "cross-sectional study" or "cross-sectional analysis" or "cross-sectional survey" or "cross-sectional design" or "prevalence study" or "prevalence analysis" or "prevalence survey" or "disease frequency study" or "disease frequency analysis" or "disease frequency survey" or cohort\* or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or 18 "longitudinal evaluation" or longitudinal\* or ((retrospective or "ex post facto") adj3 26782777 (study or survey or analysis or design)) or retrospectiv\* or "prospective study" or "prospective survey" or "prospective analysis" or prospectiv\* or "concurrent study" or "concurrent survey" or "concurrent analysis" or (("follow-up" or followup) adj (stud\* or survey or analysis)) or ((observation or observational) adj (study or survey or analysis)) or "case study" or "case series" or "clinical series" or "case studies" or "clinical study" or "clinical trial" or (("phase 0" or "phase 1" or "phase I" or "phase 2" or "phase II" or "phase 3" or "phase III" or "phase 4" or "phase IV") adj5 (trial or study)) or "evaluation study" or "evaluation survey" or "evaluation

analysis" or "case control study" or "case base study" or "case referrent study" or "case referent study" or "case referent study" or "case compeer study" or "case comparison study" or "matched case control" or "multicenter study" or "multicenter study" or "odds ratio" or "confidence interval" or (hazard\* adj (model\* or analys\* or regression or ratio or ratios)) or "Cox model" or "Cox multivariate analyses" or "Cox multivariate analysis" or "Cox regression" or "Cox survival analyses" or "Cox survival analysis" or "Cox survival model" or "change analysis" or ((study or trial or random\* or control\*) and compar\*)).mp.pt.

163 11497453

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# 19 17 and 18

20 (exp animals/ or exp nonhuman/) not exp humans/

((alpaca or alpacas or amphibian or amphibians or animal or animals or antelope or armadillo or armadillos or avian or baboon or baboons or beagle or beagles or bee or bees or bird or birds or bison or bovine or buffalo or buffaloes or buffalos or "c elegans" or "Caenorhabditis elegans" or camel or camels or canine or canines or carp or cats or cattle or chick or chicken or chickens or chicks or chimp or chimpanze or chimpanzees or chimps or cow or cows or "D melanogaster" or "dairy calf" or "dairy calves" or deer or dog or dogs or donkey or donkeys or drosophila or "Drosophila melanogaster" or duck or duckling or ducklings or ducks or equid or equids or equine or equines or feline or felines or ferret or ferrets or finch or finches or fish or flatworm or flatworms or fox or foxes or frog or frogs or "fruit flies" or "fruit fly" or "G mellonella" or "Galleria mellonella" or geese or gerbil or gerbils or goat or goats or goose or gorilla or gorillas or hamster or

21 hamsters or hare or hares or heifer or heifers or horse or horses or insect or insects 9871166 or jellyfish or kangaroo or kangaroos or kitten or kittens or lagomorph or lagomorphs or lamb or lambs or llama or llamas or macaque or macaques or macaw or macaws or marmoset or marmosets or mice or minipig or minipigs or mink or minks or monkey or monkeys or mouse or mule or mules or nematode or nematodes or octopus or octopuses or orangutan or "orang-utan" or orangutans or "orang-utans" or oxen or parrot or parrots or pig or pigeon or pigeons or piglet or piglets or pigs or porcine or primate or rodents or ruminant or ruminants or salmon or sheep or shrimp or slug or slugs or swine or tamarin or tamarins or toad or toads or trout or urchin or urchins or vole or voles or waxworm or waxworms or worm or worms or xenopus or "zebra fish" or zebrafish) not (human or humans or patient or patients)).ti,ab,hw,kw.

22 19 not (20 or 21)	
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limit 22 to (conference abstract or editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical

<sup>23</sup> index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in CCTR,CDSR,Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) PubMed not MEDLINE,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]

 24 from 23 keep 1
 1

 25 (22 not 23) or 24
 124

 26 remove duplicates from 25
 82

Number of Initial Results: 74 Number Included After Screening: 8 Studies identified through index searching: 18 Total Number of Included Studies Including Trials and Systematic Reviews: 30 Additional background references: 3

# **Hip injections**

Dmitri Souza, MD Index Used for Search: PubMed

Search: (steroids) AND (injection) AND (hip) Filters: Meta-Analysis, Randomized Controlled Trial, Systematic Review

(("steroidal"[All Fields] OR "steroidals"[All Fields] OR "steroidic"[All Fields] OR "steroids"[MeSH Terms] OR "steroids"[All Fields] OR "steroid"[All Fields]) AND ("inject"[All Fields] OR "injectability"[All Fields] OR "injectant"[All Fields] OR "injectates"[All Fields] OR "injectate"[All Fields] OR "injectates"[All Fields] OR "injectiole"[All Fields] OR "injectibles"[All Fields] OR "injecting"[All Fields] OR "injections"[MeSH Terms] OR "injections"[All Fields] OR "injectable"[All Fields] OR "injectables"[All Fields] OR "injections"[All Fields] OR "injects"[All Fields] OR "injectables"[All Fields] OR "injection"[All Fields] OR "injects"[All Fields]) AND ("hip"[MeSH Terms] OR "hip"[All Fields])) AND (meta-analysis[Filter] OR randomizedcontrolledtrial[Filter] OR systematicreview[Filter])

# Translations

steroids: "steroidal"[All Fields] OR "steroidals"[All Fields] OR "steroidic"[All Fields] OR "steroids"[MeSH Terms] OR "steroids"[All Fields] OR "steroid"[All Fields]

**injection:** "inject"[All Fields] OR "injectability"[All Fields] OR "injectant"[All Fields] OR "injectants"[All Fields] OR "injectate"[All Fields] OR "injectates"[All Fields] OR "injected"[All Fields] OR "injectible"[All Fields] OR "injectibles"[All Fields] OR "injecting"[All Fields] OR "injections"[MeSH Terms] OR "injections"[All Fields] OR "injectable"[All Fields] OR "injectables"[All Fields] OR "injection"[All Fields] OR "injects"[All Fields]

hip: "hip"[MeSH Terms] OR "hip"[All Fields]

Number of Initial Results: 121 Number Included After Screening: 17 Additional references from cross-referencing: 2

# Greater trochanteric pain syndrome

Honorio T. Benzon, MD

### Greater trochanteric pain syndrome

PUBMED, MeSH: "Corticosteroid injection for greater trochanteric pain syndrome" Results: 35 articles Used: 10 Greater trochanteric bursitis

PUBMED, MeSH: "Corticosteroid injection into greater trochanteric bursa" Results: 16 articles

Used: 5

# Gluteus medius/minimus tendinopathy

PUBMED, MeSH: "Corticosteroid injection for gluteus tendinopathy" Results: 11 articles Used: 2 Snapping hip syndrome

PUBMED, MeSH: "Iliopsoas bursa injection" Results: 26 articles

Used: 7

# Iliotibial band friction syndrome

PUBMED, MeSH: "Iliotibial band friction syndrome" Results: 15 articles Used: 2

# Knee injections

David A. Provenzano, MD Corticosteroids and Knee and Injection

(("adrenal cortex hormones"[MeSH Terms] OR ("adrenal"[All Fields] AND "cortex"[All Fields] AND "hormones"[All Fields]) OR "adrenal cortex hormones"[All Fields] OR "corticosteroid"[All Fields] OR "corticosteroids"[All Fields] OR "corticosteroidal"[All Fields] OR "corticosteroide"[All Fields] OR "corticosteroides"[All Fields]) AND (("knee"[MeSH Terms] OR "knee"[All Fields] OR "knee joint"[MeSH Terms] OR ("knee"[All Fields] AND "joint"[All Fields]) OR "knee joint"[All Fields]) AND ("inject"[All Fields] OR "injectability"[All Fields] OR "injectant"[All Fields] OR "injectants"[All Fields] OR "injectate"[All Fields] OR "injectates"[All Fields] OR "injected"[All Fields] OR "injectate"[All Fields] OR "injectates"[All Fields] OR "injecting"[All Fields] OR "injectate"[All Fields] OR "injections"[All Fields] OR "injecting"[All Fields] OR "injectables"[All Fields] OR "injections"[All Fields] OR "injects"[All Fields] OR "injectables"[All Fields] OR "injections"[All Fields] OR "injects"[All Fields] OR "injectables"[All Fields] OR "injection"[All Fields] OR "injects"[All Fields] OR "injectables"[All Fields] OR "injection"[All Fields] OR "injects"[All Fields]] OR "injectables"[All Fields] OR "injection"[All Fields] OR "injects"[All Fields]] OR "injectables"[All Fields] OR "injection"[All Fields] OR "injects"[All Fields]] OR review[Filter] OR metaanalysis[Filter] OR randomizedcontrolledtrial[Filter] OR review[Filter] OR systematicreview[Filter]] Number of initial results: 419 Number included after screening: 45

# Technique for Steroid Injections for Small Joints for Chronic Pain

Ameet Nagpal, MD, MS, MEd, MBA Index Used for Search: PubMed Search Terms Used:

 (((((steroids OR Corticosteroids OR Adrenal Cortex Hormones OR Cortisone OR Dexamethasone OR prednisolone OR Glucocorticoids OR methylprednisolone OR betamethasone) AND (injection OR injectable)) AND (small joints OR hand OR wrist OR foot OR ankle)) AND (english[Filter])) NOT ((((steroids OR Corticosteroids OR Adrenal Cortex Hormones OR Cortisone OR Dexamethasone OR prednisolone OR Glucocorticoids OR methylprednisolone OR betamethasone) AND (injection OR injectable)) AND (small joints OR hand OR wrist OR foot OR ankle)) AND ((animal[Filter]) AND (english[Filter]))) NOT (knee OR shoulder OR elbow OR hip) -Filters applied: Meta-Analysis, Randomized Controlled Trial, Systematic Review Number of Initial Results: 340

Number Included After Screening: 32

# Post Injection Protocols to Optimize Efficacy and Safety

Ameet Nagpal, MD, MS, Med, MBA

Index Used for Search: PubMed Search Terms Used:

- 1. "steroid injection" AND "joint" AND "activity" 39
- 2. "steroid injection" AND "joint" AND "rest" 17
- 3. "joint injection" and "activity" 26
- 4. "joint injection" and "rest" 6
- 5. "steroid injection" and "joint" and "prognostic factors" 2
- 6. "steroid injection" and "joint" and "weight bearing" 3
- Number of Initial Results: 39+17+26+6+2+3

Number Included After Screening: 8

# Joint Injections: Safety, Adverse Effects and Monitoring

Christine L. Hunt, DO

John FitzGerald, MD, PhD

A comprehensive search of several databases from 2001 to April 28th, 2021, any language, was conducted. The databases included Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, and Daily, Ovid EMBASE, Ovid Cochrane Central Register of Controlled Trials, and Ovid Cochrane Database of Systematic Reviews. The search strategy was designed and conducted by an experienced librarian with input from the study's principal investigator. Controlled vocabulary supplemented with keywords was used to search for studies of monitoring for adverse effects of intra-articular injected steroids in patients. The actual strategy listing all search terms used and how they are combined is available in the appendix. The systematic literature review was supplemented with references derived from prior systematic literature reviews and articles from the experts' personal libraries.

Studies broadly comparing the efficacy and/or safety of IAS to a comparator group that did not independently report the incidence of adverse effects in the IAS group were not included in our analysis.

### Pharmacokinetics of joint steroid injections

Honorio T. Benzon, MD Index Used for Search: PubMed Search Terms Used: "pharmacokinetics of steroid injection, shoulder joint" Results: 11; 1 included "pharmacokinetics of steroid injection, elbow joint" Results: 0 "pharmacokinetics of steroid injection, hip joint" Results: 2; none included "pharmacokinetics of steroid injection, knee joint" Results: 26; 2 included "pharmacokinetics of steroid injection, small joints" Results: 11; none included