Efficacy and safety of corticosteroid and other injections in the management of tendinopathy: A systematic review and meta-analysis of randomised controlled trials.

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Abstract

Background

An increasing number of injection options are available to treat tendinopathy, for which medical practitioners have little evidence-based treatment guidelines.

Methods

Randomised trials investigating local injections for tendinopathy were analysed for pain (primary outcome), function and overall patient-reported improvement, as well as adverse events. Two independent reviewers using a modified PEDro scale assessed study quality and included studies scoring greater than 50%. Meta-analyses were performed using a random effects model.

Findings

41 trials met inclusion criteria. We found strong evidence that corticosteroid injection was beneficial in the short-term but inferior to most comparisons in the intermediate and long term. Serious adverse events were infrequent, however corticosteroid injection was significantly associated with lower limb atrophy. For lateral epicondylalgia, moderate evidence of a large beneficial effect on lateral epicondylalgia was demonstrated for sodium hyaluronate (short/intermediate/long-term), botulinum toxin (short-term) and prolotherapy (intermediate-term). On direct comparison, corticosteroid injection was superior in the short-term, while platelet-rich plasma injection was superior in the intermediate and long-term. For lower limb tendinopathy, we found evidence of an inconsistent effect of polidocanol injection and no effect of platelet-rich plasma and aprotinin.

Interpretation

Current evidence suggests corticosteroid injections provide effective short-term relief of pain for most tendinopathies, however early relief must be balanced against long-term negative outcomes. Promising late outcomes are found using platelet-rich plasma, prolotherapy and sodium hyaluronate injections in lateral epicondylalgia. As response to injection varies between sites of tendinopathy, clinicians should not generalise study findings from one site to another.

Introduction

Overuse disorders of tendon or tendinopathies affect young active individuals as well as the middle aged and are often difficult to manage successfully. The currently accepted pathology is one of angiofibroblastic hyperplasia,[1] which includes hypercelluarlity, neovascularisation, increased protein synthesis and disorganisation of matrix, but not inflammation,[2-4] The latter, along with separately reported poor long-term outcomes[5] and adverse effects[6, 7] has led to questioning the ongoing use of corticosteroid injections[8] and appears to have contributed to popularisation of other injection types, such as polidocanol, platelet-rich plasma, botulinum toxin and proteinases. The growing number of studies of these other injection types underpins the need for a synthesis of the evidence for injection therapies.

The objectives of this review were to (1) investigate the clinical efficacy and risk of adverse events of injections, including corticosteroid, in the treatment of tendinopathy; (2) compare the efficacy over time (short-term, intermediate and long-term) and (3) compare the relative efficacy of injections for different sites of tendinopathy.

Methods

This meta-analysis was conducted and reported according to the Cochrane Collaboration[9] and PRISMA[10] guidelines.

Study selection

A systematic literature search was performed without language, publication or year restrictions in March 2010 in Medline, Cinahl, Embase, Web of Knowledge, Allied and Complementary Medicine, SPORTDiscus, Cochrane Controlled Trial Register and Physiotherapy Evidence Database, using the following search terms: ("Tennis Elbow"[Mesh] OR "Achilles Tendon"[Mesh] OR "Patellar Ligament"[Mesh] OR "Tendinopathy"[Mesh] OR "Tendon Injuries"[Mesh] OR "Rotator Cuff"[Mesh] OR "Shoulder Impingement Syndrome"[Mesh] OR epicondyl* OR golfers elbow OR supraspin* OR jumpers knee) AND ("Injections"[Mesh] OR "Steroids"[Mesh] OR "Anesthetics, Local"[Mesh] OR "Sclerosing Solutions"[Mesh] OR "Aprotinin"[Mesh] OR "Platelet-Rich Plasma"[Mesh] OR "Botulinum Toxins"[Mesh] OR "Glycosaminoglycans"[Mesh]). Reference lists were hand-searched for additional citations.

Inclusion criteria

Randomised controlled trials (RCT) that compared one or more peritendinous injections with placebo or other interventions for tendinopathy were included. Intramuscular or intraarticular injections were considered outside the scope of this review because the pathology in tendinopathy is regarded to occur at the tendon. Rotator cuff tendinopathy was defined in a similar manner to a previous systematic review,[11] excluding studies comprising a high proportion of adhesive capsulitis, full thickness tears or rheumatological disease. Potentially relevant citations were assessed for inclusion by one investigator (BC) and confirmed by a second investigator (LB).

Quality rating scale

Quality was assessed using a modified PEDro scale by two independent, blinded investigators (BC, LB) and disagreement resolved by consensus. Very good inter-rater reliability was achieved (6.9% initial disagreement, kappa statistic 0.85). Two items were added to the original PEDro scale (www.pedro.org.au/scale_item.html), concerning consistency of timing of outcome measurement and documentation of adverse events. Studies were considered of acceptable quality for inclusion in this review if they scored greater than 50%, which is the mean PEDro score for RCT in physical therapy.[12]

Data extraction

The following pre-defined outcomes were extracted as measures of clinical efficacy: pain (primary outcome), function and overall patient-rated improvement. The incidence of all adverse events was recorded in order to evaluate treatment safety. Data was subgrouped according to duration and comparator intervention. Duration of follow-up was categorised short, intermediate and long-term as closest to 4weeks (range 0-12weeks), 6months (range 13-26weeks) and 1year (≥52weeks) respectively.[13] Comparison was made with placebo injection (saline or local anaesthetic), no-intervention (observation or wait-and-see), non-steroidal anti-inflammatory drugs (NSAID) physiotherapy, electrotherapy or orthotic devices. Data was extracted by one investigator (BC) and confirmed by a second (BV). Authors were contacted for additional data where insufficient data was provided.

Statistical analysis

Review Manager (RevMan) statistical software[14] was used to derive summary statistics using a random effects model. For dichotomous data, the point estimates of effect were represented by the relative risk (RR) and its 95% confidence interval (CI). For continuous data, the standardized mean difference (SMD) and its 95% CI was calculated by dividing the difference in mean effects between groups by the pooled standard deviation (SD).[9] If this was not possible, the SMD was calculated from the post-intervention mean scores and corresponding SD. For adverse events, we calculated the RR with its 95% CI and the number needed to harm (NNH). NNH represents the number of patients treated for the occurrence of one extra adverse event in the treatment group compared to the control group.

Point estimates of effect were considered statistically significant where confidence intervals for RR or SMD did not contain 1 or 0, respectively. The results favoured the primary injection when SMD was positive or RR greater than one, and favoured the control when SMD was negative or RR was less than one. SMD <0.5 and RR <1.25 or >0.8 were regarded as *small*, SMD 0.5 to 0.8 and RR 1.25 to 2 or 0.5 to 0.8 as *medium* and SMD >0.8 and RR >2 or <0.5 as *large*.[15]

Pooled estimates were calculated using RevMan when subgroups of trials displayed sufficient clinical and statistical ($p<0.05$) homogeneity as assessed using Cochrane's I^2 statistic.[16] Publication bias was not assessed because of the small numbers of trials that could be pooled. For outcomes that could not be pooled, the strength of evidence was guided by the following levels of scientific evidence – *strong* (consistent findings among multiple high quality RCT), *moderate* (consistent findings among multiple low quality RCT or one high quality RCT), *limited* (one low quality RCT), *conflicting* (inconsistent findings among multiple RCT) or *no evidence*.[17]

Results

Study characteristics

Figure 1 illustrates the flow of information through the systematic review resulting in the inclusion of 41 studies. Quality rating scores ranged from 2 to 13 out of a possible 13 (Table 1) and were not anatomical site dependent. 23 articles were excluded from the systematic review because of low modified PEDro scores (i.e., <50%). Only 25% of studies used practitioner blinding, while only 28% performed intention-to-treat analysis.

Details regarding the selection criteria, interventions and extracted outcome measures for eligible studies are presented in Table 2. Of the 41 included trials, 5 did not contribute to calculation of point estimates of effect for clinical efficacy, due to insufficient data,[18-20] lack of pre-defined outcomes[21] or variable measurement times[22]. In addition, data was not extracted for timepoints occurring after cross-over of the placebo group in four studies.[23-26] There were 34 short-term trials, 18 intermediate trials and 11 long-term trials. Effect statistics were calculated for pain (27 trials), function (19 trials), and overall patient-rated improvement (16 trials) for corticosteroid injection (28 trials, Table 3) or alternative injections (15 trials, Table 4). Herein we discuss only the pain outcomes for studies in which all other outcomes mirrored the pain outcomes. 35 out of 41 included trials contributed toward evaluation of adverse events.

Efficacy of corticosteroid injection for lateral epicondylalgia

Evidence for the effectiveness of corticosteroid injection for lateral epicondylalgia was based on 12 studies (Figure 2, n=1171). All study populations comprised clinically diagnosed lateral epicondylalgia of 3-6 months median duration, except for one study[27] (< four weeks). A single injection was investigated in seven trials, up to three injections in four trials and one study compared single versus repeated injections.[28]

Short-term results

Compared to non-injection interventions there was strong evidence in the short-term for corticosteroid injections across all outcome measures. Point estimates of effect were large in comparison to no-intervention (SMD 1.44, 95% CI 1.17 to 1.71[5, 29, 30]), NSAID (SMD 1.02, 95% CI 0.61 to 1.43[31]), physiotherapy[5, 29, 30, 32] and orthotic devices. [33] Although findings were consistent (largely favouring corticosteroid injections), significant heterogeneity was found for comparison with physiotherapy. Different physiotherapy protocols were utilised in each study. Significant heterogeneity was also found for the subgroup of placebo-controlled studies, limiting pooling of data. Compared to local anaesthetic injection, one trial[34] (n=87) found a large beneficial effect of corticosteroid injection on pain (SMD 0.95, 95% CI 0.41 to 1.50), while another two trials[27, 35] (n=64 and 39) found no differences. Of these two latter studies, one had a 25% loss to follow-up (even loss between groups)[35] and in the other all patients received concomitant physiotherapy.[27]A third trial, reported no difference in global improvement compared to saline injection combined with NSAID.[36] Comparison of corticosteroid injection with platelet-rich plasma injection showed a small effect on pain in favour of corticosteroid injection (SMD 0.44, 95% CI 0.04 to 0.84[37]).

Intermediate-term results

There is a strong trend that corticosteroid injections are inferior to other interventions at six months. Negative effects on pain were found following corticosteroid injection compared to no-intervention (SMD -0.4, 95% CI -0.67 to -0.14[5, 29]), NSAID (SMD -0.52, 95% CI -0.92 to -0.13[31]) and physiotherapy (SMD -0.56, 95% CI -0.82 to -0.31[5, 29]) and platelet-rich plasma injection (SMD -0.86, 95% CI -1.27 to -0.45[37]).

Long-term results

Ongoing negative effects on pain were identified one year following corticosteroid injection compared to no-intervention (SMD -0.31, 95% CI -0.61 to -0.01[5, 29]), platelet-rich plasma injection (SMD -0.83, 95% CI -1.24 to -0.42) and physiotherapy (SMD -0.48, 95% CI -0.73 to -0.23[5, 29]), but not when compared to NSAID where there was no difference.[31]

Effect of different corticosteroid injection parameters

Doses and suspensions of corticosteroid did not appear to alter outcomes,[34] though this has not been thoroughly evaluated. However, repeated corticosteroid injections (average 4.3 injections, range 3-6, over 18 months) resulted in a larger negative long-term effect on pain (SMD -10.11, 95% CI -12.20 to -8.01) compared to a single injection.[28]

Efficacy of corticosteroid injection for medial epicondylalgia

Only one trial[38] (n=60) investigating corticosteroid injection compared to placebo injection for medial epicondylalgia met the criteria for inclusion. It found no short-term effect of corticosteroid injection on a visual analogue score of pain (SMD 0.43, 95% CI -0.08 to 0.94[38]), but a medium beneficial effect on a composite measure of pain and function (Nirschl and Pettrone Pain Phase). No differences were found at one year (SMD 0.10, 95% CI -0.4 to 0.61).

Efficacy of corticosteroid injection for rotator cuff tendinopathy

Thirteen trials investigated the effectiveness of corticosteroid injection for rotator cuff tendinopathy (figure 3, n=890; omitting 3 trials[18, 19, 22] with insufficient data). The mean duration of symptoms varied from less than four weeks in 82% of patients in one trial[39] to 3.2 years in another trial.[40] Population characteristics were found to differ between included studies (Table 2). Eligibility was based on a clinical diagnosis in 7 out of 13 (54%) trials, while the remaining trials utilised X-ray, ultrasound or magnetic resonance imaging to confirm exclusion criteria, such as rotator cuff tears, calcification and arthritic change. In eight (62%) trials, inclusion was based on a substantial relief of symptoms following subacromial injection of local anaesthetic.

Short-term results

Overall, evidence for the short-term efficacy of corticosteroid injections for rotator cuff tendinopathy is conflicting. Pooling of three small studies comparing corticosteroid to placebo injection found a medium beneficial effect of corticosteroid injection on pain (SMD

0.68, 95% CI 0.35 to 1.01[40-42]). A large effect was also observed in comparison to Tenoxicam (NSAID) injection[43] for global improvement (RR 1.54, 95% CI 1.02 to 2.33) and function (SMD 0.98, 95% CI 0.42 to 1.54). In contrast, no difference in effect was demonstrated in all studies where oral NSAID[39, 41, 42, 44-46] were prescribed. Trials comparing corticosteroid injection to physiotherapy, found no differences in pain[47] or function,[46] although significantly greater numbers of patients reported complete recovery following corticosteroid injection at 6 weeks (RR 3.06, 95% CI 1.27 to 7.39[47]).

Intermediate and long-term results

No significant differences were demonstrated in all studies of intermediate[40, 44-47] and long-term outcomes[46] following corticosteroid injection for rotator cuff tendinopathy.

Effect of different corticosteroid injection parameters

Comparison of local and systemic injection sites for rotator cuff tendinopathy failed to find significant differences in short-term outcome.[48] Other dose parameters have not been studied in rotator cuff tendinopathy.

Efficacy of corticosteroid injection for Achilles and Patellar tendinopathy

Two trials[21, 26] investigated corticosteroid injection for lower limb tendinopathy, however only one trial[26] presented sufficient data for analysis. Corticosteroid injection was compared with placebo injection in a small (n=48) study of chronic (≥6months) mid-substance Achilles and patellar tendinopathy with ultrasound changes including tendon thickening and absence of partial or total rupture.[26] A large short-term effect on pain was demonstrated in favour of corticosteroid injection (SMD 0.81, 95% CI 0.22 to 1.4). On a subgroup analysis of tendon sites, a beneficial effect was seen for patellar tendons (SMD 0.91, 95% CI 0.06 to 1.76), but not for Achilles tendons (SMD 0.73, 95%CI -0.11 to 1.56), though the latter approached statistical significance.

Efficacy of alternative injections for tendinopathy

Fifteen trials investigated injections other than corticosteroid medication, however two of these did not use predefined outcomes of interest.[20, 21] Comparison was made with placebo injection (10trials, Figure 4), eccentric exercise (one trial[49]) and electrotherapy modalities (one trial[50]). Direct comparison between corticosteroid and platelet-rich plasma injection was made in one study,[37] while another trial compared different doses of polidocanol.[51] The number of injections varied from a single injection to five, weekly injections.[52]

Ultrasound-guided injection of polidocanol, a sclerosing solution, was compared with saline injection in three trials.[23-25] A large overall improvement was found for patellar tendinopathy at 16 weeks (SMD 1.69, 95% CI 0.88 to 2.50; n=33), [24] while outcomes did not reach significance for Achilles tendinopathy (n=20).[23] No difference was found for any measures for lateral epicondylalgia in the short-term(n=36).[25] Different doses of polidocanol in Achilles tendinopathy were not found to significantly differ in efficacy (n=52).[51]

Platelet-rich plasma was investigated in two recent trials.[37, 53] It did not differ on any outcomes in the short or intermediate-term, when compared with placebo injection in chronic (≥2months) mid-substance Achilles tendinopathy (n=54).[53] Direct comparison was made

between corticosteroid and platelet-rich plasma injection for chronic (>6months), severe (>50/100 pain visual analogue scale) lateral epicondylalgia in the other study (n=100).[37] In the short-term, corticosteroid injection was minimally favourable (SMD 0.44, 95% CI 0.04 to 0.84),[37] whereas platelet-rich plasma injection was largely favourable in the intermediate (SMD -0.86, 95% CI -1.27 to -0.45) and long-term (SMD -0.83, 95% CI -1.24 to -0.42). Placebo comparison was not performed in this study.

Prolotherapy injection was studied in two small trials.[49, 54] The first study[54] (n=24) compared a series of three injections over an eight week period with placebo injection for chronic (average duration 1.9years) lateral epicondylalgia. While no effect was seen at eight weeks (immediately prior to the third injection), a large effect on pain was found at 16 weeks (SMD 2.62, 95% CI 1.36, 3.88). The other study (n=43) investigated a series of four to 12 prolotherapy injections in clinical and ultrasound diagnosed Achilles tendinopathy (> 6-weeks duration). Compared to eccentric exercise, prolotherapy or a combination of prolotherapy and eccentric exercise, was not found to differ on any outcomes over a 12 month period.[49] Placebo comparison was not performed in this study.

Sodium hyaluronate was also studied in two trials.[50, 55] In comparison to placebo injection for lateral epicondylalgia, sodium hyaluronate was highly superior in relieving pain in the short-term (SMD 3.91, 95% CI 3.54 to 4.28), intermediate (SMD 2.89, 95% CI 2.58 to 3.2) and long-term (SMD 3.91, 95% CI 3.55 to 4.28). No short-term benefit was observed for any outcomes in comparison to electrotherapy modalities for rotator cuff tendinopathy (n=50).[50]

Comparison with placebo injection was made in a single trial of arteparon,[52] aprotinin,[56] and botulinum toxin.[57] No significant short-term or intermediate effects on pain were demonstrated for a series of five, weekly injections of arteparon, a glycosaminoglycan polysulphate solution, for lateral epicondylalgia (n=65). [52] A series of three, weekly injections of the proteinase, aprotinin (n=33) also demonstrated no beneficial short or long-term effect on any outcomes for Achilles tendinopathy.[56] Wong et al (n=60) investigated peritendinous injection of botulinum toxin in chronic lateral epicondylalgia (average duration 1.25years).[57] A large effect on pain was demonstrated in the short-term (SMD 1.23, 95% CI 0.67 to 1.78) in comparison to placebo injection.

Adverse events

All trials of alternative injections reported adverse events, whereas only 25/30 trials (83%) did so for corticosteroid injection (Table 3). Overall event rates were calculated by summing the numbers of events reported in each of the included studies that reported adverse event data. In addition, RR and NNH scores were calculated for studies with placebo injection comparison.

Of the 991 patients treated with corticosteroid injection, there were 53 cases of subcutaneous atrophy (5.3%), 12 cases of depigmentation (1.2%), 21 cases of facial flushing (2.1%) and 1 case of tendon rupture (0.1%), which occurred after two corticosteroid injections into the Achilles tendon.[26] On comparison to placebo injection, there was a significant relative risk of atrophy for Achilles and patellar tendons[26] (RR 20.9 (95%CI 1.32 to 332; NNH 2), but not for elbow tendons[34] (RR 1.77, 95% CI 0.73 to 4.29, NNH 8).

No adverse events, except pain were observed following injection of 97 patients with polidocanol,[23-25, 51] 356 patients treated with sodium hyaluronate,[50, 55] 40 patients treated with prolotherapy[49, 54] or 78 patients treated with platelet-rich plasma.[37, 53] Significantly greater harm was found for injections of both botulinum toxin and aprotinin when compared to placebo injection. Aprotinin injection was associated with a significant relative risk of itching[56] (5.40, 95% CI 1.97 to 14.81; NNH 3) and burning[21] (3.08, 95% CI 1.24 to 7.64; NNH 3). Botulinum Toxin was associated with a significant relative risk of total adverse events compared to saline injection[57] (2.11, 95% CI 1.15 to 3.89; NNH 3), which was likely attributable to greater reports of weakness (33%) and paresis (13%).

Injection-related pain varied between trials and the type of placebo injection. Post-injection pain was reported more frequently following corticosteroid injection than local anaesthetic (NNH 5),[34] while more frequently for saline injection than corticosteroid injection (NNH 39).[21] In one study,[54] 100% of patients receiving a series of five injections of either prolotherapy or saline solutions reported pain. Gastrointestinal disorders, vertigo and rash were more common following placebo injection combined with oral NSAID use than corticosteroid injection[42]or arteparon injection.[20]

Discussion

An increasing number of injections are available to treat tendinopathy, challenging practitioners to stay abreast of new evidence and make informed clinical decisions regarding choice of therapy. This is the first review to synthesise the evidence from higher quality randomised trials, evaluating the likelihood and magnitude of benefit and harm for different injections across all common tendinopathies. It highlights the disparity in the strength of scientific evidence for many injection therapies. Based on the current available evidence, we can be confident in our conclusions regarding corticosteroid injections for lateral epicondylalgia, however further research is necessary to confirm conclusions regarding corticosteroid injection for lower limb and rotator cuff tendinopathy and all other injection types.

Corticosteroid injections, a potent anti-inflammatory intervention,[58] present as a clinical dilemma because there is consistent evidence of its short-term superior effect across a number of high quality RCT, yet tendinopathy is widely regarded not to involve an inflammatory pathology. The biological basis for the effect of corticosteroid injection on tendinopathy is unclear, with altered release of noxious chemicals and inhibition of collagen, extracellular matrix molecules and granulation tissue potential contributors.[58] This systematic review challenges its ongoing use by providing strong evidence of the long-term inferiority of corticosteroid injections compared to most conservative interventions for tendinopathy. Based on 12 studies, strong evidence of a large, beneficial effect of corticosteroid injection was demonstrated for lateral epicondylalgia in the short-term (< 8 weeks), which is in agreement with previous meta-analyses.[59, 60] While previously alluded to, our meta-analysis now confirms negative outcomes at six months, which are still evident one year following corticosteroid injection for lateral epicondylalgia. From 10 trials of rotator cuff tendinopathy, evidence of an inconsistent effect of corticosteroid injection was drawn. Analysis of a subgroup of three studies, found a medium beneficial effect in comparison to placebo injection alone, which concurs with previous meta-analyses.[59, 61] There is moderate evidence from one small high quality trial[26] for the short-term efficacy of corticosteroid injection for lower limb tendinopathy, however benefits may be limited to patellar tendons and to the short-term, given many showed relapse within six months, which is a similar trend to lateral

epicondylalgia. In clinical practice, corticosteroid injection is commonly prescribed in combination with NSAID or physiotherapy. No difference in effect was found for corticosteroid compared to placebo injection for all studies where NSAID[42, 44, 45] or physiotherapy[27, 30] were prescribed as a co-intervention. This is not that unexpected because these treatments produce beneficial effects, and in so doing thereby reduce the available amount of improvement to be gained by injections, either drug or placebo. Future studies of sufficient size are needed to determine if physiotherapy can reduce the high recurrences associated with corticosteroid injection.[62, 63]

Despite the growing popularity of novel injection therapies for tendinopathy, there remains many unanswered questions regarding their therapeutic efficacy and physiological basis. Recent research has focussed on injection of substances aimed at obliterating areas of neovascularisation within affected tendons. This review demonstrated ultrasound-guided injection of polidocanol was not more effective than placebo for treating lateral epicondylalgia,[25] but may be of benefit in chronic lower limb tendinopathy (moderate evidence)[23, 24]. Prolotherapy injection, comprising a solution of hypertonic glucose and local anaesthetic, was effective in the intermediate term for lateral epicondylalgia,[54] while a series of 4-12 prolotherapy injections (either alone or in combination with eccentric exercise) was not more effective than eccentric exercise alone (moderate evidence).[49] Administration of growth factors to stimulate tendon healing has also gained interest. Direct comparison of platelet-rich plasma with corticosteroid injection for lateral epicondylalgia demonstrated superior outcomes of corticosteroid in the short-term, while platelet-rich plasma were superior in the intermediate and long-term (moderate evidence).[37] Its benefit over placebo for lateral epicondylalgia is not known, while it was not more effective than placebo for Achilles tendinopathy.[53] No randomised trials were found for injection of autologous blood for treating tendinopathy. Petrella et al studied injection of sodium hyaluronate, a naturally occurring biological substance, and reported that it was largely effective over a 12 month period for chronic severe lateral epicondylalgia (n = 331, moderate evidence).[55] However, they also reported no improvement in the placebo group over twelve months, which is inconsistent with the majority of placebo-controlled studies of lateral epicondylalgia. There is moderate evidence that arteparon (glycosaminoglycan polysulphate) and aprotinin (proteinase) injections, both proposed to inhibit enzymes that degrade tendon ground substance, are not more effective than placebo injection.[52, 56] Botulinum toxin injection into the painful area 1 cm from the lateral epicondyle was largely effective in the short-term for lateral epicondylalgia (moderate evidence).[57] Widely used for neurological disorders when it is injected into muscle, the underlying mechanism in tendon has yet to be elucidated.

Clinically there is a dictum that a potentially catastrophic effect of injecting into a tendon is the weakening of tendon and increased likelihood of rupture. Previous review of ten animal studies examining the effects of corticosteroid injections on tendons, did not find conclusive evidence as to whether corticosteroid injections do or do not cause damage to tendons.[64] We found a low incidence of serious adverse events following corticosteroid injection (only one case of tendon rupture), which suggests an acceptable level of risk. While in agreement with other authors,[59, 64, 65] more rigorous assessment and reporting of adverse events across trials is needed to confirm the safety of corticosteroid injections. Minor complications including post-injection pain, subcutaneous atrophy and skin depigmentation were common, with the relative risk of reversible lower limb atrophy being significantly greater following corticosteroid injection. Moderate evidence was found to support the harmful effects of repeated corticosteroid injection on pain.[28] However the critical number of corticosteroid injections or the critical interval between injections before harms outweigh benefits is not

known. Patients and practitioners wishing to make an informed choice regarding corticosteroid injection, are strongly urged to consider other consequences of treatment that may not be defined as adverse, including negative long-term outcomes and higher recurrence rates.[5, 29] Unique adverse event profiles were found for alternative injection therapies. Polidocanol, prolotherapy, arteparon, sodium hyaluronate and platelet-rich plasma injections were well tolerated. Greater risk of burning and itching were associated with aprotinin injection, supply of which was suspended in 2007 following clinical trials associated it with an increased risk of death.[66] Finger weakness and paresis were more common following botulinum toxin injection 1cm from the lateral epicondyle, symptoms suggestive of neuromuscular involvement.

We limited this review to randomised trials to improve the likelihood of an unbiased assessment. Analysis of trials regardless of quality did not significantly change the conclusions of this review. Corticosteroid injection was found to be more effective in the short-term compared to placebo injection,[67] NSAID,[68] shock wave therapy,[69] elbow band,[70] or physiotherapy[71] for lateral epicondylalgia and compared to placebo injection for medial epicondylalgia.[72] No difference was found in the short-term between corticosteroid injection and eccentric or heavy slow resistance training in chronic (≥3months) patellar tendinopathy.[73] However, corticosteroid injection was associated with inferior functional outcomes at six months[73] (SMD -0.98, 95% CI -1.76 to -0.20), reflecting a common pattern of corticosteroid injections.

Injections were found to differ in both clinical efficacy and adverse events between tendon sites, despite what is commonly reported to be a similar pathology.[74] As many trials were restricted to selected subgroups of tendinopathy, application of any findings to clinical practice will therefore involve a degree of judgement. Difficulty associated with diagnosis of tendinopathy may account for heterogeneity of outcomes, particularly of the rotator cuff, where variation in eligibility criteria was evident between trials (see Table 2). Ultrasound imaging of tendon morphology is proposed to reduce the heterogeneity of included populations.[26] Six out of nine trials of the lower limb utilised ultrasound to confirm diagnosis, while ultrasound examinations were performed in only one study of lateral epicondylalgia [25] and rotator cuff tendinopathy.[48] Notably, only one third of athletes with clinically suspected Achilles or patellar tendinopathy were confirmed to have ultrasonically determined thickening (>1mm) of the symptomatic tendon.[26] Further longitudinal research is needed to confirm whether ultrasound abnormalities correlate with clinical recovery.[75] Poor response to injection or side-effects, including raised intratendinous pressure, tendon degeneration and deleterious effects on intraarticular cartilage, may be due to a misplaced injection. Ultrasound-guided injection was performed in all four studies of polidocanol, to target areas of neovascularisation within the extensor tendon at the lateral elbow,[25] or outside the Achilles and patellar tendons.[23, 24, 51] It is not known whether the differing protocols for injection contribute to findings. In two studies, ultrasound-guided corticosteroid injection was used to avoid direct injection into the Achilles, patellar[26] or rotator cuff[48] tendons. However, no difference in accuracy was found between blinded and ultrasound-guided subacromial injections, raising debate regarding its clinical utility.[76]

This comprehensive systematic review and meta-analysis allows a rigorous appraisal of the evidence for the efficacy and harms of different injections for tendinopathy. Whilst we can be confident in the short-term efficacy of corticosteroid injection for many tendon conditions, its long-term inefficacy must not be ignored. Further research into alternative injections, in particular platelet-rich plasma, prolotherapy, polidocanol and sodium hyaluronate is

warranted to confirm their clinical utility. Greater attention must be given in future studies to recruitment of a sufficient sample size, standardisation of co-interventions, long-term follow-up, assessment of recurrence and systematic reporting of adverse events.

Author Contribution
All authors contributed to the investigation and writing of this manuscript.

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None

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Tables and Figures:

Table 1: Quality rating scores using the modified PEDro scale. Each criterion met is marked in grey.

Table 2: Characteristics of included studies, including predefined outcome measures and follow-up time points. Outcomes provided as change scores* or final value scores† and additional data supplied by authors#.
Abbreviations: Non-steroidal anti-inflammatory drugs (NSAID), Magnetic resonance imaging (MRI), Ultrasound (US), Visual Analogue Scale (VAS), Numerical Rating Scale (NRS), Victorian Institute of Sports Assessment (VISA), Patient related forearm evaluation questionnaire (PRFEQ).

Table 3: Standardised mean difference (SMD) and relative risk (RR) scores and their 95% confidence intervals (CI) of the clinical efficacy of corticosteroid injections (CSI) for tendinopathy. Pooled scores for clinically homogenous comparisons are provided along with a measure of heterogeneity (I2).

Table 4. Standardised mean difference (SMD) and relative risk (RR) scores and their 95% confidence intervals (CI) of the clinical efficacy of alternative injections for Lateral epicondylalgia (LE), Achilles (ACH), patellar (PT) and rotator cuff tendinopathy(RC).

Table 5. Incidence (%), relative risk (RR) and its 95% confidence interval (CI) and numbers needed to harm (NNH) for adverse events following experimental injections compared to placebo injection or placebo injection combined with non-steroidal anti-inflammatory drugs*****. NNH representing greater adverse events for control intervention is indicated by ^.

Figure 1. Flowchart of trials through the systematic review.

Figure 2. Standardised mean difference (SMD) and its 95% confidence interval (CI) for improvement in pain following corticosteroid injection (CSI) for lateral epicondylalgia.

Figure 3. Standardised mean difference (SMD) and its 95% confidence interval (CI) for improvement in pain following corticosteroid injection for rotator cuff tendinopathy. Where pain scores were unavailable, the SMD for improvement in function is indicated by ^.

Figure 4. Standardised mean difference (SMD) and its 95% confidence interval (CI) for improvement in pain following all injection types in comparison to placebo injection for lateral epicondylalgia (LE), medial epicondylalgia (ME), rotator cuff (RC), Achilles (ACH), and patellar tendinopathy (PT). Pooled data is provided where there is more than one study. Where pain scores were unavailable, the SMD for improvement in function is indicated by ^.

References

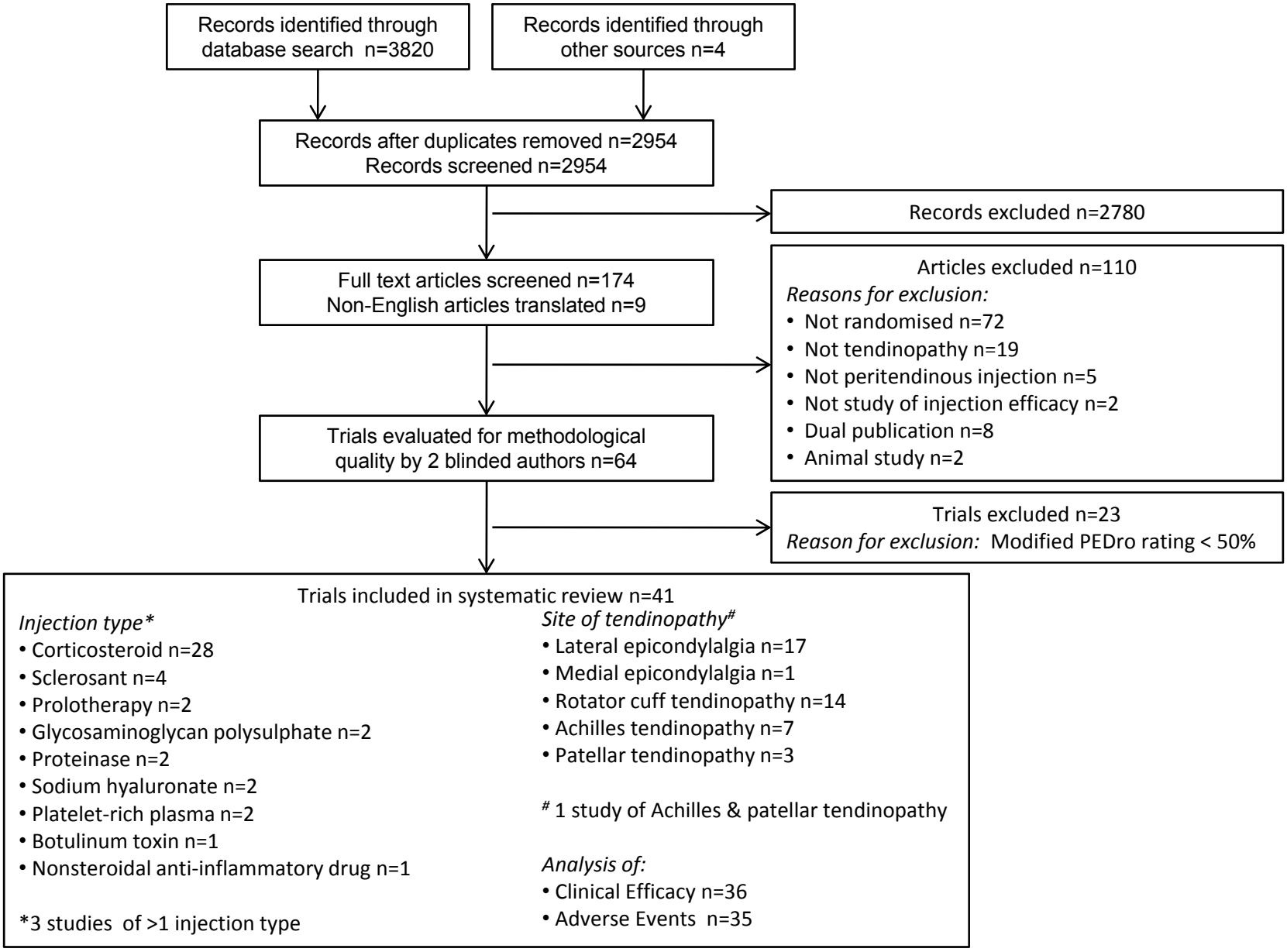
1. Kraushaar BS, Nirschl RP. Tendinosis of the elbow (tennis elbow). Clinical features and findings of histological, immunohistochemical, and electron microscopy studies. J Bone Joint Surg Am. 1999 Feb;81(2):259-78.
2. Khan KM, Cook JL, Kannus P, Maffulli N, Bonar SF. Time to abandon the "tendinitis" myth. Bmj. 2002 Mar 16;324(7338):626-7.
3. Rees JD, Maffulli N, Cook J. Management of tendinopathy. Am J Sports Med. 2009 Sep;37(9):1855-67.
4. Maffulli N, Testa V, Capasso G, Ewen SW, Sullo A, Benazzo F, et al. Similar histopathological picture in males with Achilles and patellar tendinopathy. Med Sci Sports Exerc. 2004 Sep;36(9):1470-5.
5. Bisset L, Beller E, Jull G, Brooks P, Darnell R, Vicenzino B. Mobilisation with movement and exercise, corticosteroid injection, or wait and see for tennis elbow: randomised trial. BMJ. 2006 Nov 4;333(7575):939.
6. Mahler F, Fritschy D. Partial and complete ruptures of the Achilles tendon and local corticosteroid injections. Br J Sports Med. 1992 Mar;26(1):7-14.
7. Shrier I, Matheson GO, Kohl HW, 3rd. Achilles tendonitis: are corticosteroid injections useful or harmful? Clin J Sport Med. 1996 Oct;6(4):245-50.
8. Osborne H. Stop injecting corticosteroid into patients with tennis elbow, they are much more likely to get better by themselves! J Sci Med Sport. 2009 Nov 25.
9. Higgins JPT, Green SE. Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.1 ed: The Cochrane Collaboration; 2008.
10. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med. 2009 Jul 21;6(7):e1000100.
11. Green S, Buchbinder R, Glazier R, Forbes A. Systematic review of randomised controlled trials of interventions for painful shoulder: selection criteria, outcome assessment, and efficacy. BMJ. 1998;316:354-60.
12. Maher CG, Moseley AM, Sherrington C, Elkins MR, Herbert RD. A description of the trials, reviews, and practice guidelines indexed in the PEDro database. Phys Ther. 2008 Sep;88(9):1068-77.
13. Furlan AD, Pennick V, Bombardier C, van Tulder M. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. Spine (Phila Pa 1976). 2009 Aug 15;34(18):1929-41.
14. The Nordic Cochrane Centre TCC. Review Manager (RevMan) [Computer program]. Version 5.0 ed. Copenhagen; 2008.
15. Cohen J, editor. Statistical power analysis for the behavioral sciences. Hillsdale: Lawrence Erlbaum Associateds; 1988.
16. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003 Sep 6;327(7414):557-60.
17. van Tulder M, Furlan A, Bombardier C, Bouter L. Updated method guidelines for systematic reviews in the cochrane collaboration back review group. Spine. 2003 Jun 15;28(12):1290-9.
18. McInerney JJ, Dias J, Durham S, Evans A. Randomised controlled trial of single, subacromial injection of methylprednisolone in patients with persistent, post-traumatic impingment of the shoulder. Emerg Med J. 2003 May;20(3):218-21.

19. Vecchio PC, Hazleman BL, King RH. A double-blind trial comparing subacromial methylprednisolone and lignocaine in acute rotator cuff tendinitis. Br J Rheumatol. 1993 Aug;32(8):743-5.
20. Sundqvist H, Forsskahl B, Kvist M. A promising novel therapy for Achilles peritendinitis: double-blind comparison of glycosaminoglycan polysulfate and high-dose indomethacin. Int J Sports Med. 1987 Aug;8(4):298-303.
21. Capasso G, Testa V, Maffuli N, Bifulco G. Aprotinin, corticosteroids and normosaline in the management of patellar tendinopathy in athletes: a prospective randomised study. Sports Exercise and Injury. 1997;3:111-5.
22. Blair B, Rokito AS, Cuomo F, Jarolem K, Zuckerman JD. Efficacy of injections of corticosteroids for subacromial impingement syndrome. J Bone Joint Surg Am. 1996 Nov;78(11):1685-9.
23. Alfredson H, Ohberg L. Sclerosing injections to areas of neo-vascularisation reduce pain in chronic Achilles tendinopathy: a double-blind randomised controlled trial. Knee Surg Sports Traumatol Arthrosc. 2005 May;13(4):338-44.
24. Hoksrud A, Ohberg L, Alfredson H, Bahr R. Ultrasound-guided sclerosis of neovessels in painful chronic patellar tendinopathy: a randomized controlled trial. Am J Sports Med. 2006 Nov;34(11):1738-46.
25. Zeisig E, Fahlstrom M, Ohberg L, Alfredson H. Pain relief after intratendinous injections in patients with tennis elbow: results of a randomised study. Br J Sports Med. 2008 Apr;42(4):267-71.
26. Fredberg U, Bolvig L, Pfeiffer-Jensen M, Clemmensen D, Jakobsen BW, Stengaard-Pedersen K. Ultrasonography as a tool for diagnosis, guidance of local steroid injection and, together with pressure algometry, monitoring of the treatment of athletes with chronic jumper's knee and Achilles tendinitis: a randomized, double-blind, placebo-controlled study. Scand J Rheumatol. 2004;33(2):94-101.
27. Newcomer KL, Laskowski ER, Idank DM, McLean TJ, Egan KS. Corticosteroid injection in early treatment of lateral epicondylitis. Clin J Sport Med. 2001 Oct;11(4):214-22.
28. Okcu G, Yercan H, Ozic U. The comparison of single dose versus multi-dose local corticosteroid injections for tennis elbow. Klinik Arastirma / Clinical Research. 2002;13(3):158-63.
29. Smidt N, van der Windt DA, Assendelft WJ, Deville WL, Korthals-de Bos IB, Bouter LM. Corticosteroid injections, physiotherapy, or a wait-and-see policy for lateral epicondylitis: a randomised controlled trial. Lancet. 2002 Feb 23;359(9307):657-62.
30. Tonks JH, Pai SK, Murali SR. Steroid injection therapy is the best conservative treatment for lateral epicondylitis: a prospective randomised controlled trial. Int J Clin Pract. 2007 Feb;61(2):240-6.
31. Hay EM, Paterson SM, Lewis M, Hosie G, Croft P. Pragmatic randomised controlled trial of local corticosteroid injection and naproxen for treatment of lateral epicondylitis of elbow in primary care. BMJ. 1999 Oct 9;319(7215):964-8.
32. Verhaar JA, Walenkamp GH, van Mameren H, Kester AD, van der Linden AJ. Local corticosteroid injection versus Cyriax-type physiotherapy for tennis elbow. J Bone Joint Surg Br. 1996 Jan;78(1):128-32.
33. Haker E, Lundeberg T. Elbow-band, splintage and steroids in lateral epicondylalgia (tennis elbow). The Pain Clinic. 1993;6(2):103-12.
34. Price R, Sinclair H, Heinrich I, Gibson T. Local injection treatment of tennis elbow--hydrocortisone, triamcinolone and lignocaine compared. Br J Rheumatol. 1991 Feb;30(1):39-44.

35. Lindenhovius A, Henket M, Gilligan BP, Lozano-Calderon S, Jupiter JB, Ring D. Injection of dexamethasone versus placebo for lateral elbow pain: a prospective, double-blind, randomized clinical trial. J Hand Surg [Am]. 2008 Jul-Aug;33(6):909-19.
36. Saartok T, Eriksson E. Randomized trial of oral naproxen or local injection of betamethasone in lateral epicondylitis of the humerus. Orthopedics. 1986 Feb;9(2):191-4.
37. Peerbooms JC, Sluimer J, Bruijn DJ, Gosens T. Positive Effect of an Autologous Platelet Concentrate in Lateral Epicondylitis in a Double-Blind Randomized Controlled Trial : Platelet-Rich Plasma Versus Corticosteroid Injection With a 1-Year Follow-up. Am J Sports Med. 2010;38:255.
38. Stahl S, Kaufman T. The efficacy of an injection of steroids for medial epicondylitis. A prospective study of sixty elbows. J Bone Joint Surg Am. 1997 Nov;79(11):1648-52.
39. White RH, Paull DM, Fleming KW. Rotator cuff tendinitis: comparison of subacromial injection of a long acting corticosteroid versus oral indomethacin therapy. J Rheumatol. 1986 Jun;13(3):608-13.
40. Alvarez CM, Litchfield R, Jackowski D, Griffin S, Kirkley A. A prospective, double-blind, randomized clinical trial comparing subacromial injection of betamethasone and xylocaine to xylocaine alone in chronic rotator cuff tendinosis. Am J Sports Med. 2005 Feb;33(2):255-62.
41. Adebajo AO, Nash P, Hazleman BL. A prospective double blind dummy placebo controlled study comparing triamcinolone hexacetonide injection with oral diclofenac 50 mg TDS in patients with rotator cuff tendinitis. J Rheumatol. 1990 Sep;17(9):1207-10.
42. Petri M, Dobrow R, Neiman R, Whiting-O'Keefe Q, Seaman WE. Randomized, double-blind, placebo-controlled study of the treatment of the painful shoulder. Arthritis Rheum. 1987 Sep;30(9):1040-5.
43. Karthikeyan S, Kwong HT, Upadhyay PK, Parsons N, Drew SJ, Griffin D. A double-blind randomised controlled study comparing subacromial injection of tenoxicam or methylprednisolone in patients with subacromial impingement. J Bone Joint Surg Br. 2010 Jan;92(1):77-82.
44. Akgun K, Birtane M, Akarimak U. Is local subacromial corticosteroid injection beneficial in subacromial impingement syndrome? Clin Rheumatol. 2004;23:496-500.
45. Alvarez-Nemegyei J, Bassol-Perea A, Pasos J. Efficacy of the local injection of methylprednisolone acetate in the subacromial impingement syndrome. A randomised, double blind trial. Reumatol Clin. 2008;4(2):49-54.
46. Cloke DJ, Watson H, Purdy S, Steen IN, Williams JR. A pilot randomized, controlled trial of treatment for painful arc of the shoulder. J Shoulder Elbow Surg. 2008 Jan-Feb;17(1 Suppl):17S-21S.
47. Hay EM, Thomas E, Paterson SM, Dziedzic K, Croft PR. A pragmatic randomised controlled trial of local corticosteroid injection and physiotherapy for the treatment of new episodes of unilateral shoulder pain in primary care. Ann Rheum Dis. 2003 May;62(5):394-9.
48. Ekeberg OM, Bautz-Holter E, Tveita EK, Juel NG, Kvalheim S, Brox JI. Subacromial ultrasound guided or systemic steroid injection for rotator cuff disease: randomised double blind study. BMJ. 2009;338:a3112.
49. Yelland MJ, Sweeting KR, Lyftogt JA, Ng SK, Scuffham PA, Evans KA. Prolotherapy injections and eccentric loading exercises for painful Achilles tendinosis: a randomised trial. Br J Sports Med. 2009 Sep 6.
50. Sengul I, Oz B, Yoleri O, Olmez N, Memis A, Uluc E. Sodium Hyaluronate Injections Compared to Local Modalities for the Treatment of Shoulder Impingement Syndrome. Turk J Phys Med Rehab. 2008;54:138-42.
51. Willberg L, Sunding K, Ohberg L, Forssblad M, Fahlstrom M, Alfredson H. Sclerosing injections to treat midportion Achilles tendinosis: a randomised controlled study

evaluating two different concentrations of Polidocanol. Knee Surg Sports Traumatol Arthrosc. 2008 Sep;16(9):859-64.
52. Akermark C, Crone H, Elsasser U, Forsskahl B. Glycosaminoglycan polysulfate injections in lateral humeral epicondylalgia: a placebo-controlled double-blind trial. Int J Sports Med. 1995 Apr;16(3):196-200.
53. de Vos RJ, Weir A, van Schie HT, Bierma-Zeinstra SM, Verhaar JA, Weinans H, et al. Platelet-rich plasma injection for chronic Achilles tendinopathy: a randomized controlled trial. JAMA. 2010 Jan 13;303(2):144-9.
54. Scarpone M, Rabago DP, Zgierska A, Arbogast G, Snell E. The efficacy of prolotherapy for lateral epicondylosis: a pilot study. Clin J Sport Med. 2008 May;18(3):248-54.
55. Petrella RJ, Cogliano A, Decaria J, Mohamed N, Lee R. Management of Tennis Elbow with sodium hyaluronate periarticular injections. Sports Med Arthrosc Rehabil Ther Technol. 2010;2:4.
56. Brown R, Orchard J, Kinchington M, Hooper A, Nalder G. Aprotinin in the management of Achilles tendinopathy: a randomised controlled trial. Br J Sports Med. 2006 Mar;40(3):275-9.
57. Wong SM, Hui AC, Tong PY, Poon DW, Yu E, Wong LK. Treatment of lateral epicondylitis with botulinum toxin: a randomized, double-blind, placebo-controlled trial. Ann Intern Med. 2005 Dec 6;143(11):793-7.
58. Paavola M, Kannus P, Jarvinen TA, Jarvinen TL, Jozsa L, Jarvinen M. Treatment of tendon disorders. Is there a role for corticosteroid injection? Foot Ankle Clin. 2002 Sep;7(3):501-13.
59. Gaujoux-Viala C, Dougados M, Gossec L. Efficacy and safety of steroid injections for shoulder and elbow tendonitis: A meta-analysis of randomized controlled trials. Ann Rheum Dis. 2008 Dec 3.
60. Smidt N, Assendelft WJ, van der Windt DA, Hay EM, Buchbinder R, Bouter LM. Corticosteroid injections for lateral epicondylitis: a systematic review. Pain. 2002 Mar;96(1-2):23-40.
61. Buchbinder R, Green S, Youd JM. Corticosteroid injections for shoulder pain. Cochrane Database Syst Rev. 2003(1):CD004016.
62. Coombes BK, Bisset L, Connelly LB, Brooks P, Vicenzino B. Optimising corticosteroid injection for lateral epicondylalgia with the addition of physiotherapy: a protocol for a randomised control trial with placebo comparison. BMC Musculoskelet Disord. 2009;10:76.
63. Olaussen M, Holmedal O, Lindbaek M, Brage S. Physiotherapy alone or in combination with corticosteroid injection for acute lateral epicondylitis in general practice: a protocol for a randomised, placebo-controlled study. BMC Musculoskelet Disord. 2009;10:152.
64. Nichols AW. Complications associated with the use of corticosteroids in the treatment of athletic injuries. Clin J Sport Med. 2005 Sep;15(5):370-5.
65. Gill SS, Gelbke MK, Mattson SL, Anderson MW, Hurwitz SR. Fluoroscopically guided low-volume peritendinous corticosteroid injection for Achilles tendinopathy. A safety study. J Bone Joint Surg Am. 2004 Apr;86-A(4):802-6.
66. Therapeutic Goods Administration. Safety information - Trasylol (aprotinin) injection. 2007 [cited; Available from: http://www.tga.gov.au/alerts/trasylol.htm
67. Erdum HR, Erturk C, Akalin C, Tetik S, Uner NK, Koca I. Comparison of local injection treatment of lateral epicondylitis with methylprednisolone, triamcinolone and local anesthetic injections. Romatizma Arastirma Ve Savas Dernegi Der Ankara. 1995;10(2):90-5.

68. Toker S, Kilincoglu v, Aksakalli E, Gulcan E, Ozkan K. Short-term results of treatment of tennis elbow with anti-inflammatory drugs alone or in combination with local injection of a corticosteroid and anaesthetic mixture. Acta Orthop Et Traumatologica Turcica. 2008;42(3):184-7.
69. Crowther MA, Bannister GC, Huma H, Rooker GD. A prospective, randomised study to compare extracorporeal shock-wave therapy and injection of steroid for the treatment of tennis elbow. J Bone Joint Surg Br. 2002 Jul;84(5):678-9.
70. Erturk H, Celiker R, Sivri A, Cetin A, Cindas A. The efficacy of different treatment regiments that are commonly used in tennis elbow. J Rheum Med Rehab. 1997;8(4):298-301.
71. Boghemans J. The efficacy of depo-medrone in sports injuries. Acta Belg Med Phys. 1984 Apr-Jun;7(2):47-50.
72. Bahari M, Gharehdaghi M, Rahimi H. Injection of methylprednisolone and lidocaine in the treatment of medial epicondylitis: A randomized clinical trial. Iranian Medicine. 2003;6(3):196-9.
73. Kongsgaard M, Kovanen V, Aagaard P, Doessing S, Hansen P, Laursen AH, et al. Corticosteroid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. Scand J Med Sci Sports. 2009 Sep 28.
74. Khan KM, Cook JL, Bonar F, Harcourt P, Astrom M. Histopathology of common tendinopathies. Update and implications for clinical management. Sports Med. 1999 Jun;27(6):393-408.
75. Cook JL, Khan KM, Kiss ZS, Coleman BD, Griffiths L. Asymptomatic hypoechoic regions on patellar tendon ultrasound: A 4-year clinical and ultrasound followup of 46 tendons. Scand J Med Sci Sports. 2001 Dec;11(6):321-7.
76. Rutten MJ, Maresch BJ, Jager GJ, de Waal Malefijt MC. Injection of the subacromial-subdeltoid bursa: blind or ultrasound-guided? Acta Orthop. 2007 Apr;78(2):254-7.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Records excluded n=2780
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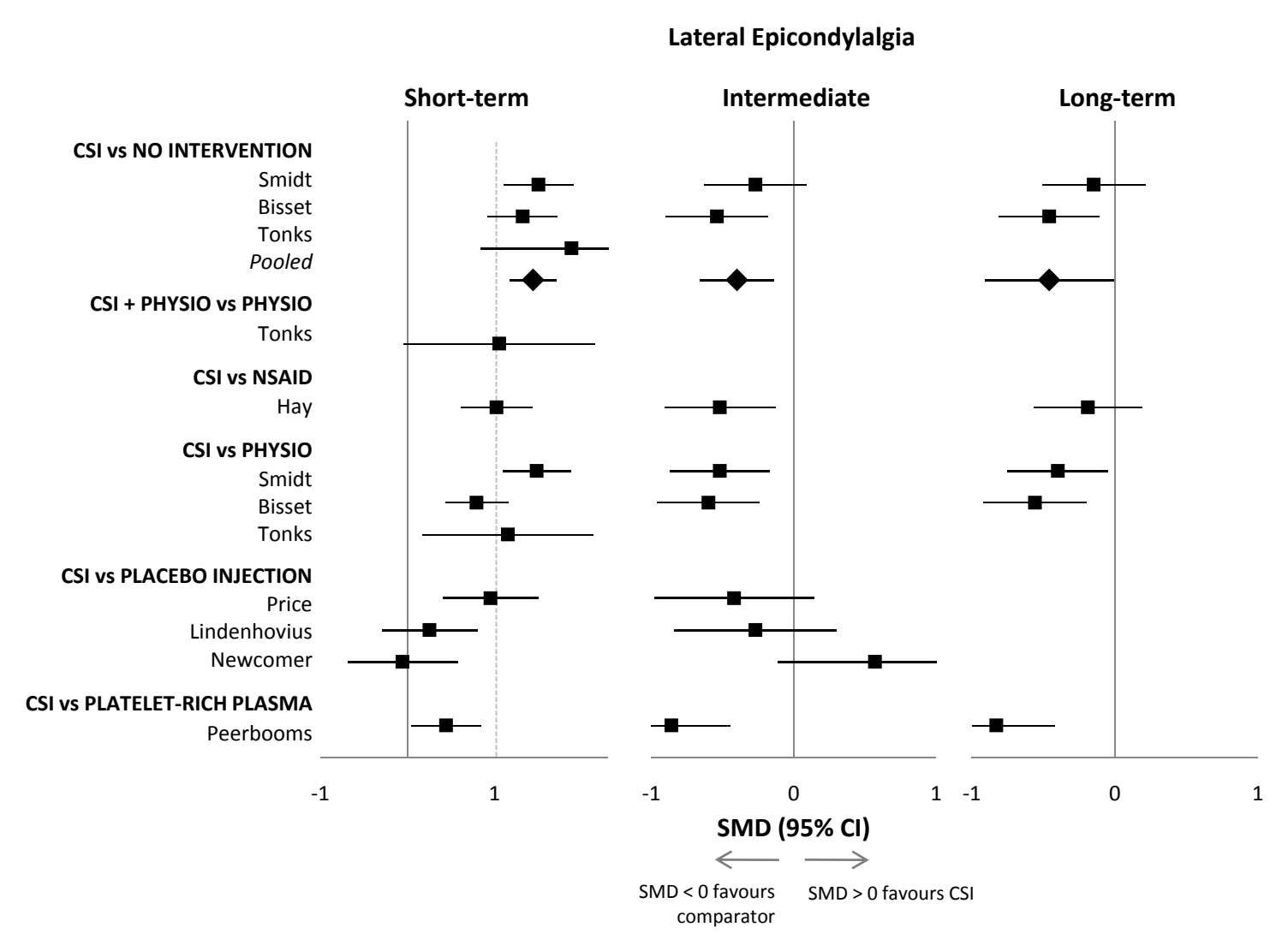
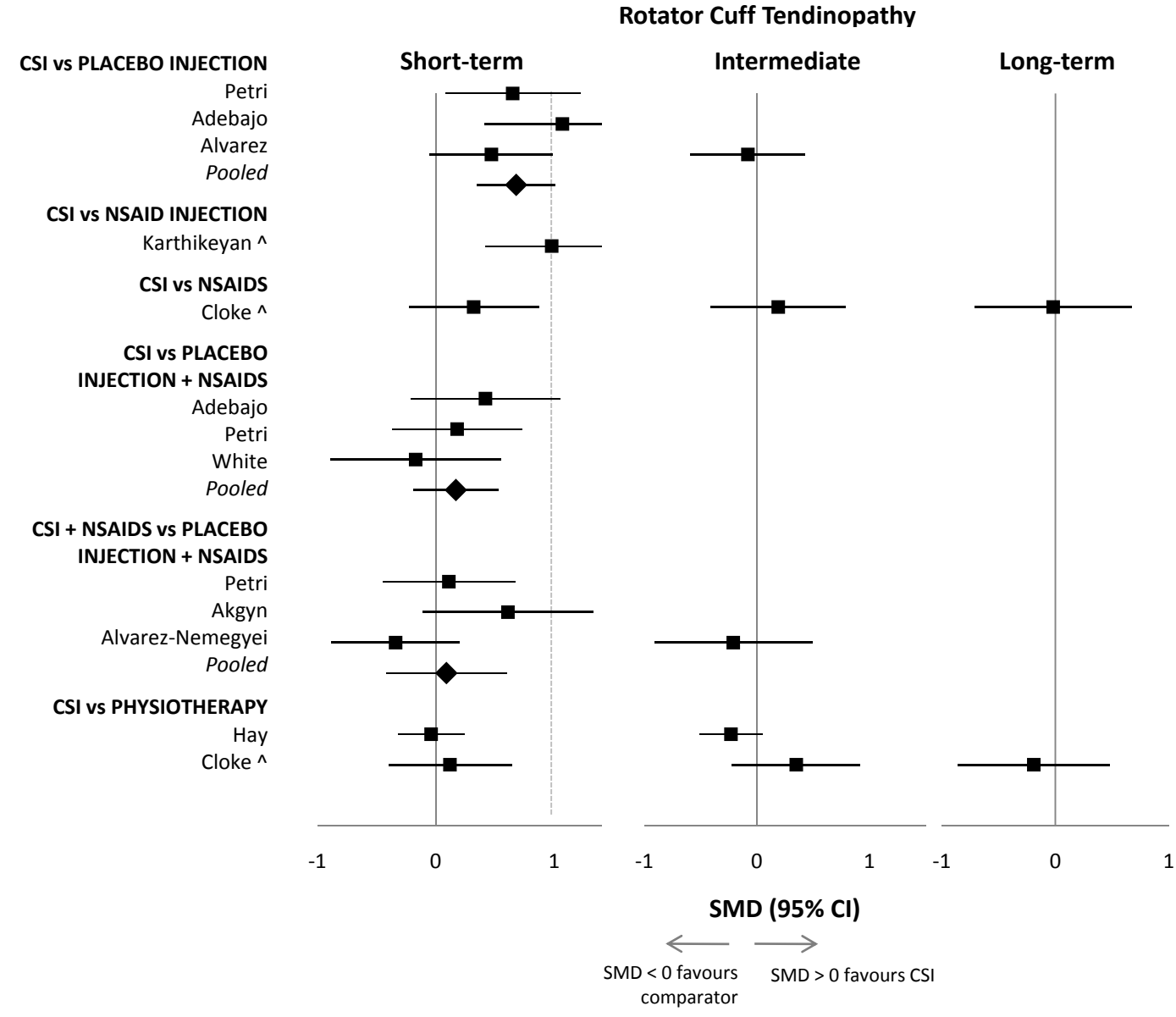
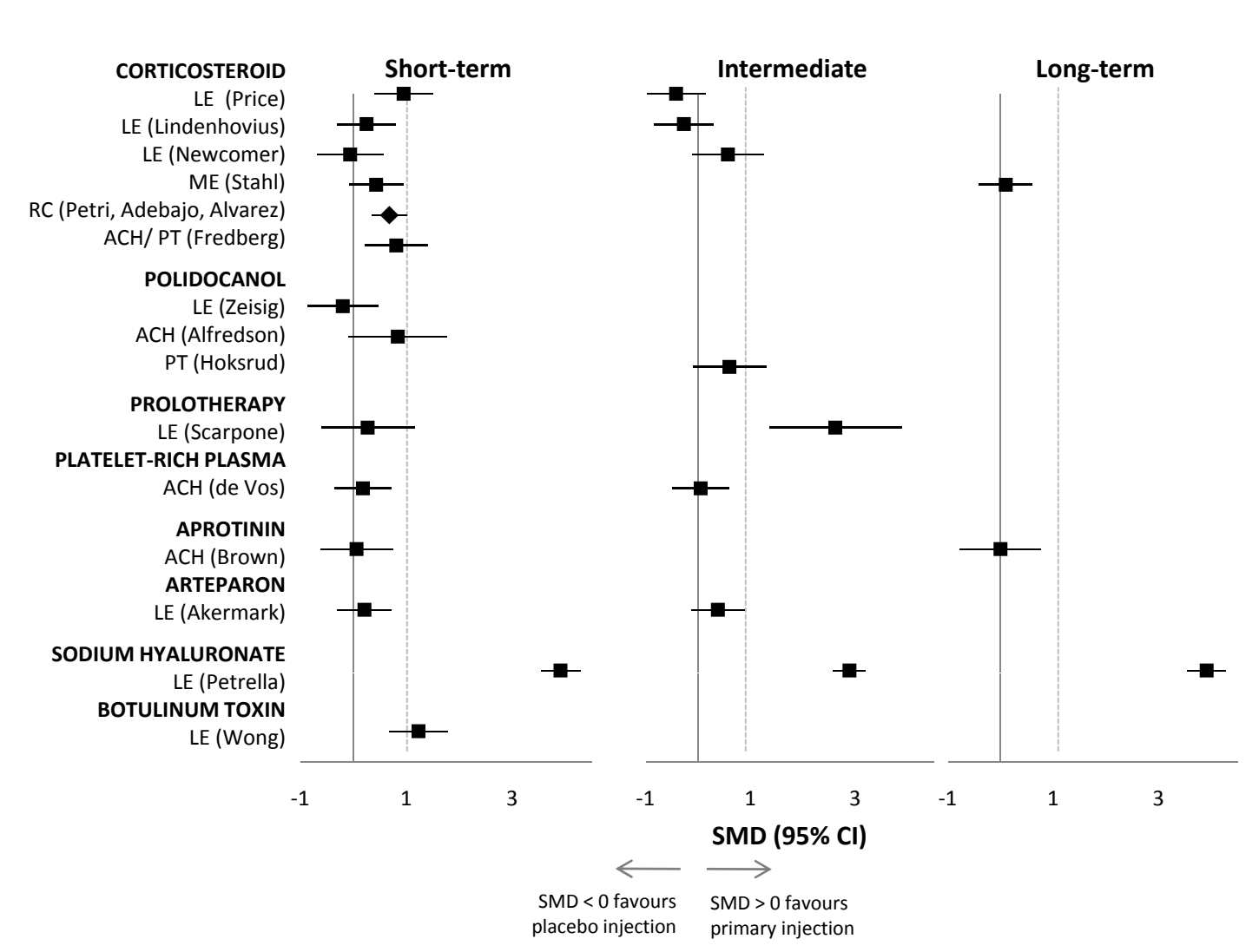
Articles excluded n=110
Reasons for exclusion:
• Not randomised n=72
• Not tendinopathy n=19
• Not peritendinous injection n=5
• Not study of injection efficacy n=2
• Dual publication n=8
• Animal study n=2
Trials evaluated for methodological quality by 2 blinded authors n=64
Trials excluded n=23
Reason for exclusion: Modified PEDro rating < 50%
Trials included in systematic review n=41
Injection type*
• Corticosteroid n=28
• Sclerosant n=4
• Prolotherapy n=2
• Glycosaminoglycan polysulphate n=2
• Proteinase n=2
• Sodium hyaluronate n=2
• Platelet-rich plasma n=2
• Botulinum toxin n=1
• Nonsteroidal anti-inflammatory drug n=1
*3 studies of >1 injection type
Site of tendinopathy#
• Lateral epicondylalgia n=17
• Medial epicondylalgia n=1
• Rotator cuff tendinopathy n=14
• Achilles tendinopathy n=7
• Patellar tendinopathy n=3
1 study of Achilles & patellar tendinopathy
Analysis of:
• Clinical Efficacy n=36
• Adverse Events n=35


Lateral Epicondylalgia
Short-term
Intermediate
Long-term
CSI vs NO INTERVENTION
Smidt
Bisset
Tonks
Pooled
CSI + PHYSIO vs PHYSIO
Tonks
CSI vs NSAID
Hay
CSI vs PHYSIO
Smidt
Bisset
Tonks
CSI vs PLACEBO INJECTION
Price
Lindenhovius
Newcomer
CSI vs PLATELET-RICH PLASMA
Peerbooms
-1
1
-1
0
1
-1
0
1
SMD (95% CI)
SMD < 0 favours comparator
SMD > 0 favours CSI


Rotator Cuff Tendinopathy
Short-term
Intermediate
Long-term
CSI vs PLACEBO INJECTION
Petri
Adebajo
Alvarez
Pooled
CSI vs NSAID INJECTION
Karthikeyan ^
CSI vs NSAIDS
Cloke ^
CSI vs PLACEBO INJECTION + NSAIDS
Adebajo
Petri
White
Pooled
CSI + NSAIDS vs PLACEBO INJECTION + NSAIDS
Petri
Akgyn
Alvarez-Nemegyei
Pooled
CSI vs PHYSIOTHERAPY
Hay
Cloke ^
-1
0
1
SMD (95% CI)
SMD < 0 favours comparator
SMD > 0 favours CSI


CORTICOSTEROID
LE (Price)
LE (Lindenhovius)
LE (Newcomer)
ME (Stahl)
RC (Petri, Adebajo, Alvarez)
ACH/ PT (Fredberg)
POLIDOCANOL
LE (Zeisig)
ACH (Alfredson)
PT (Hoksrud)
PROLOTHERAPY
LE (Scarpone)
PLATELET-RICH PLASMA
ACH (de Vos)
APROTININ
ACH (Brown)
ARTEPARON
LE (Akermark)
SODIUM HYALURONATE
LE (Petrella)
BOTULINUM TOXIN
LE (Wong)
Short-term
Intermediate
Long-term
-1
1
3
SMD (95% CI)
SMD < 0 favours placebo injection
SMD > 0 favours primary injection

Author (year)	1 Eligibility	2 Random allocation	3 Concealed allocation	4 Baseline similarity	5 Subject blinding	6 Therapist blinding	7 Assessor blinding	8 85% follow up	9 Intention to treat	10 Between-group statistics	11 Point/variability measure	12 Outcome timing similarity	13 Adverse effect data	Total Score (%)	Review Inclusion
Lateral Epicondylalgia															
Akermark (1995)	■	■		■	■	■	■	■		■	■	■	■	85	Y
Bar (1997)		■												46	N
Bisset (2006)	■	■	■	■			■	■	■	■	■	■	■	85	Y
Boghemans (1984)		■								■				15	N
Crowther (2002)	■	■	■							■	■	■		46	N
Erdum (1995)	■	■		■			■					■	■	46	N
Erturk (1997)	■	■		■						■		■		38	N
Freeland (1954)		■			■		■	■						31	N
Haker (1993)	■	■						■		■	■	■	■	54	Y
Halle (1986)	■	■						■		■		■	■	31	N
Hay (1999)	■	■		■			■	■	■	■	■	■	■	77	Y
Jensen (2001)	■	■	■							■	■	■		46	N
Lindenhovius (2008)	■	■	■	■	■	■	■	■	■	■	■		■	85	Y
Mandiroglu (207)	■	■								■	■	■	■	46	N
Newcomer (2001)	■	■		■	■	■	■	■	■	■	■	■		85	Y
Okcu (2002)	■	■								■	■	■	■	54	Y
Peerboom (2010)	■	■	■		■	■	■			■	■	■	■	77	Y
Petrella (2010)	■	■		■	■				■	■		■	■	62	Y
Price (1991)	■	■		■	■		■	■	■	■	■	■	■	85	Y
Saartok (1986)	■	■			■			■		■	■	■	■	62	Y
Scarpone (2008)		■	■	■	■	■			■	■	■	■	■	77	Y
Smidt (2002)	■	■	■	■			■	■	■	■	■	■	■	85	Y
Solveborn (1995)		■								■		■	■	23	N
Toker (2008)		■						■		■	■	■	■	46	N
Tonks (2007)	■	■	■	■						■	■	■	■	62	Y
Verhaar (1996)	■	■	■					■		■	■	■	■	69	Y
Wong (2005)	■	■	■	■	■	■	■	■		■	■	■	■	92	Y
Zeisig (2008)	■	■	■	■	■	■	■	■		■	■	■	■	92	Y
Medial Epicondylalgia															
Bahari (2003)	■	■								■	■	■	■	46	N
Stahl (1997)		■						■		■	■	■	■	85	Y
Rotator Cuff Tendinopathy															
Adebajo (1990)	■	■		■	■		■	■		■	■	■	■	77	Y
Akgyn (2004)		■		■	■		■	■		■	■	■	■	69	Y
Alvarez (2005)		■	■	■	■	■	■	■	■	■	■	■		85	Y
Alvarez-Nemegyei (2008)	■	■		■	■	■	■	■		■	■	■	■	69	Y
Berry (1980)	■	■	■	■			■	■			■	■	■	62	Y
Blair (1996)	■	■	■	■	■		■	■		■	■		■	62	Y
Cloke (2008)	■	■	■						■	■	■	■		54	Y
Ekeberg (2009)	■	■	■	■	■		■	■	■	■	■	■	■	92	Y
Hay (2003)	■	■	■	■			■	■	■	■	■	■		77	Y
Karthikeyan (2010)	■	■		■	■	■	■			■	■	■	■	85	Y
McInerney (2003)	■	■	■	■			■	■	■	■		■	■	77	Y
Meloni (2007)		■										■	■	23	N
Petri (1987)	■	■		■	■	■	■	■		■	■	■	■	85	Y
Plafki (2000)	■	■					■					■		31	N
Pons (2001)	■	■									■		■	31	N
Şengül (2008)		■	■	■				■		■	■	■	■	54	Y
Strobel (1996)		■								■		■	■	31	N
Ulreich (1996)		■										■		15	N
Vecchio (1993)	■	■		■	■	■	■	■		■	■	■	■	69	Y
White (1986)	■	■			■					■	■	■	■	54	Y
Withrington (1985)		■			■		■			■		■		38	N
Yilmaz (2008)		■										■		15	N
Achilles Tendinopathy															
Alfredson (2005)		■	■		■	■	■	■		■	■		■	69	Y
Brown (2006)	■	■		■	■	■	■			■		■	■	69	Y
DaCruz (1988)	■	■		■								■	■	38	N
De Vos (2010)	■	■	■		■	■	■	■	■	■	■	■	■	92	Y
Pforringer (1994)		■	■	■	■					■		■	■	46	N
Sundqvist (1987)		■						■		■	■	■	■	54	Y
Willberg (2008)	■	■	■	■	■	■	■	■		■	■		■	77	Y
Yelland (2009)	■	■	■	■	■	■	■	■	■	■	■	■	■	77	Y
Achilles and Patellar Tendinopathy															
Fredberg (2004)	■	■						■		■		■	■	69	Y
Patellar Tendinopathy															
Capasso (1997)		■								■	■		■	54	Y
Hoksrud (2006)	■	■	■	■	■	■	■	■	■	■	■	■	■	100	Y
Kongsgaard (2009)		■		■							■	■	■	46	N
Kvist (1982)		■						■		■	■	■	■	46	N

Table 2

	PEDro	Population Characteristics	Interventions (number randomised)	Outcome Measures/*Timepoints*
Corticosteroid Injection for Lateral Epicondylalgia (LE)				
Bisset (2006)	11/13	Clinical diagnosis of unilateral LE >6weeks; Exclusion: treatment previous 6months, other elbow pathology, radiculopathy, nerve involvement, surgery, fracture, dislocation, neurological disorders, medication contraindication; Mean pain VAS 57/100	i. 1ml Triamcinolone Acetonide 10mg/ml +1ml 1% Lidocaine, 1-2 injections, 2week interval (n=65) ii. Physiotherapy (n=66) 8x30minute sessions, elbow mobilisation with movement, concentric /eccentric /isometric /general arm exercise ii. Wait-and-see (n=67)	Pain VAS (0-100) * Pain-free function scale (/100) * Global improvement (complete recovery or much improved) (6 point scale) Adverse events *6, 26, 52 weeks*
Haker (1993)	7/13	Clinical diagnosis of LE >1month; Exclusion: neck/ shoulder dysfunction, arthritis, neurological abnormality, nerve entrapment	i. 0.2ml Triamcinolone Acetonide 10mg/ml + 0.3ml Bupivicaine Hydrochloride (1-2 injections, 1week interval) (n=19) ii. Elbow band for 3months (n=18) iii. Wrist splint for 3months (n=19)	Patient perceived change (excellent or good) (5 point scale) Adverse events *2, 26, 52 weeks*
Hay (1999)	10/13	Clinical diagnosis of LE (new episode), Exclusion: arthritis, gross structural abnormality, medication contraindication; Mean NRS 5.1/9	i. 20mg Methylprednisolone + 0.5ml 1% Lignocaine single injection (n=53) ii. 500mg Naproxen 2/day for 2weeks (n=53) iii. Placebo tablet, 2/day for 2weeks (n=58)	Pain NRS (0-9) † Impairment of function NRS (0-9)† Global improvement (complete recovery) (5 point scale) Adverse events *4, 26, 52 weeks*
Linden-hovius (2008)	11/13	LE <6months, clinical diagnosis with substantial relief following Lidocaine injection; Exclusion: surgery, inflammatory disease, pregnancy, limited elbow motion, neurological signs, previous steroid use	i. 1ml 4mg Dexamethasone + 1ml 1% Lidocaine without Epinephrine (n=31) ii. 2ml 1% Lidocaine without Epinephrine injection (n=33); single injection, Co-intervention allowed	Pain VAS (0-10) † Disabilities of the Shoulder, Arm and Hand (DASH) scale (/100) † Adverse events *4, 26 weeks*
Newcomer (2001)	11/13	Clinical diagnosis of acute, unilateral LE <4weeks; Exclusion: previous treatment, nerve entrapment, history of trauma or past LE, inflammatory disorders, workers compensation, systemic steroids	i. 5ml Betamethasone (6ml/ml) + 0.25% Bupivacaine Hydrochloride (n=20) ii. 5ml 0.25% Bupivicaine Hydrochloride (n=19) Single injection, Co-intervention: Rehabilitation comprising strength/ stretch exercise, ice	Pain VAS (0-100) * # *4, 26 weeks*
Okcu (2002) [Turkish]	7/13	Clinical diagnosis of LE; Exclusion: steroid injection previous year, inflammatory disorders, cervical origin, elbow trauma; Mean pain VAS 83/100	0.5ml 4.53mg Bethamethasone+0.5ml 5mg Prilocain i. Single injection (n=22) ii. Multiple injections (n=30) (minimum 4week intervals; mean 4.3 injections at 18months) Co-intervention: NSAID Tilcotil 20mg/day for 10days	Pain VAS (0-100) † Subjective satisfaction (pleased) (3 point scale) Adverse events *6, 78 weeks*
Peer-booms (2010)	10/13	Clinical diagnosis of LE>6months and pain VAS >50/100, normal X-ray; Exclusion: <18years, pregnancy, history of carpal tunnel, cervical radiculopathy, systemic disorders eg diabetes, rheumatoid arthritis, hepatitis, steroid injection or surgery in past 6 months; Mean pain VAS 67/100	i. 4ml 40mg/ml Triamcinolon Acetonide (Kenacort) + Bupivacaine Hydrochloride 0.5% with Epinephrine (n=49) ii.4ml Platelet-rich plasma injection (n=51) Single injection with peppering technique Co-intervention: Physiotherapy: rest 24hours, stretching 2 weeks, followed by eccentric strengthening exercise	Pain VAS (0-100) † Disabilities of the Shoulder, Arm and Hand (DASH) scale † Adverse events *4, 26 and 52 weeks*
Price (1991)	11/13	Clinical Diagnosis of LE, previous treatment accepted Mean pain VAS *Study 1.* 49/100 Mean pain VAS *Study 2.* 65/100	*Study 1.* i. 2ml 10mg Triamcinolone + 1% Lignocaine (n=29) ii. 2ml 25mg Hydrocortisone + 1% Lignocaine (n=29) iii. 2ml of 1% Lignocaine (n=29) *Study 2.* i. 2ml 10mg Triamcinolone + 1% Lignocaine (n=23) ii. 2ml 20mg Triamcinolone + 1% Lignocaine (n=28)	Pain VAS (0-100) † Adverse events *4, 24 weeks*
Saartok (1986)	8/13	Clinical diagnosis of LE; Exclusion: treatment within previous 5weeks	i. 1ml 6mg Betamethasone + 0.5ml 1% Prilocaine, single injection + placebo tablets (n=11) ii. 1.5ml Saline injection + 250mg NSAID Naproxen 2/day, initial dose 500mg for 2weeks (n=10)	Patient perceived evaluation (cured or markedly improved) (6 point scale) Adverse events *2 weeks*
Smidt (2002)	11/13	Clinical diagnosis of unilateral LE >6weeks; Exclusion: injections or physiotherapy previous 6months, radiculopathy, elbow deformity, surgery, trauma,neurological disorders, medication contraindication; Median day pain 60/100	i. 1ml Triamcinolone Acetonide 10mg/ml + 1ml 2% Lidocaine, 1-3 injections over 6weeks (n=62) ii. Physiotherapy: 8x30minute sessions, US, friction massage, stretches, strength/ occupational exercise (n=64) iii. Wait-and-see (n=59)	Pain during day NRS (0-100) * Modified Pain-free Function Scale (/100)* Global improvement (complete recovery or much improved) (6 point scale) Adverse events *3, 26, 52 weeks*
Tonks (2007)	8/13	Clinical diagnosis of unilateral LE; Exclusion: treatment previous 6months; cervical or other upper limb pathology, trauma, surgery, systemic steroids, injection contraindication	i. 1ml Triamcinolone Acetonide 10mg/ml +2% Lignocaine hydrochloride single injection (n=12) ii. 1ml Triamcinolone Acetonide 10mg/ml +2% Lignocaine hydrochloride + Physiotherapy (n=12) ii. Physiotherapy: Strength/ stretch exercise (n=12) iii. Observation (n=12)	Patient rated forearm evaluation questionnaire (PRFEQ) Pain subscale (0-50) * PRFEQ Function subscale (0-100)* Adverse events *7 weeks*
Verhaar (1996)	9/13	Clinical diagnosis of LE; Exclusion: surgery, arthritis, neurological disorder, >3 steroid injections previous 6months, previous Cyriax treatment	i. 1ml 1% Triamcinolone Acetate +1ml 1% Lidocaine (1-3injections, 2week intervals) (n=53) ii. Cyriax Physiotherapy (n=53) 12 sessions over 4weeks, transverse friction massage, Mills manipulation; Co-intervention: combination therapy (20%); surgery (30%)	Patient perceived satisfaction (satisfied) (3 point scale) Adverse events *6, 52 weeks*

	PEDro	Population Characteristics	Interventions (number randomised)	Outcome Measures/*Timepoints*
Corticosteroid Injection for Rotator Cuff Tendinopathy (RC)				
Adebajo (1990)	10/13	Acute (<3months) RC tendinitis: painful arc, pain with resisted abduction or rotation, passive motion normal; Exclusion: systemic inflammation, glenohumeral or acromioclavicular arthritis, bicipital tendinitis, suspected RC tear; Mean pain VAS 6.5/10	i. 1ml 80mg/ml Triamcinolone Hexacetonide + 2ml 0.5% Lignocaine + placebo tablet (n=20) ii. 3ml 0.5% Lignocaine + NSAID Diclofenac 50mg (n=20) iii. 3ml 0.5% Lignocaine + placebo tablet (n=20) Single injection; Tablets 3/day for 28days; Co-intervention: Pendular/ wall climb exercise	Pain VAS (0-10) * Limitation of function (0-3) * Adverse events *4 weeks*
Akgyn (2004)	9/13	Clinical and magnetic resonance imaging (MRI) diagnosis of subacromial impingement syndrome: positive impingement tests, positive subacromial injection test, MRI stage 2; Exclusion: MRI stage 3 (complete tear); frozen shoulder, calcific tendonitis, dislocation, cervical pain, fibromyalgia, treatment in previous 3months; Mean activity pain with activity VAS 6/10	i. 40mg Methylprednisolone + 10cc 1% Lignocaine + 500mg NSAID Naproxen Sodium (n=16) ii. 10cc 1% Lignocaine + 500mg NSAID Naproxen Sodium (n=16); 2 injections, 10day interval; NSAIDS 2/day for 15days; Co-intervention: Pendular/ strength/ stretch exercise	Activity Pain VAS (0-10) † Total Constant Score (Function) (0-100) † *4 weeks*
Alvarez (2005)	11/13	Chronic (>6months) tendinosis or partial cuff tear; pain on palpation of cuff insertion, decreased or painful shoulder motion, positive Neer impingement sign; positive subacromial injection test, failed 2week trial NSAIDS, failed 6week physical therapy; Exclusion: full thickness tear on ultrasound; Mean pain VAS with Neers Test 58/100	i. 1ml 6mg Betamethasone (Celestone Soluspan) + 4ml 2% Xylocaine (n=31) ii. 5ml 2% Xylocaine (n=31) Single injection	Pain with Neers test VAS (0-100) † Disabilities of the Shoulder, Arm and Hand (DASH) scale † 2, *26 weeks*
Alvarez-Nemegyei (2008) [Spanish]	9/13	RC tendinitis, positive subacromial lidocaine injection test; Exclusion: Acromioclavicular sprain or osteophytes, calcium deposits on X-ray, allergy, rheumatological disease, hypertension or uncontrolled diabetes; Mean Pain VAS 57.5 /100	i. 2ml 40mg/ml Methylprednisolone Acetate + 1ml 1% Lidocaine (n=27) ii. 3ml 1% Lidocaine (n=29) Co-intervention:'Standard' physiotherapy rehabilitation and NSAIDS	Pain VAS (0-100) * # Shoulder Disability Questionnaire (0-23) * Adverse events *4, 24 weeks*
Blair (1996)	8/13	Subacromial impingement syndrome >3months, positive Lidocaine Injection test; Exclusion: previous steroid injection, os acromiale on X-Ray, Workers' Compensation claim, full thickness tear (contrast arthrography)	i. 2ml of 40mg/ml Triamcinolone Acetonide + 4ml 1% Lidocaine without Epinephrine (n=19) ii. 6ml 1% Lidocaine without Epinephrine (n=21) single subacromial injection; Co-intervention: Physical therapy: pasive/ assisted/ active/ Theraband strength exercise	Patient perception of pain change (decreased pain) (3point scale) - data not extracted due to range of follow-up 12-55weeks (mean 30) Adverse events
Cloke (2008)	7/13	Painful arc with active shoulder abduction <6months; Exclusion: neck referred pain, systemtic inflammatory arthritis, severe loss of motion (capsulitis), glenohumeral or acromioclavicular arthritis, incompetant RC (marked weakness), injection in previous 3months, medication contraindication	i. 40mg Methylprednisolone + 10ml 1% Lidocaine, 3 injections, 6week intervals (n=27) ii. NSAIDS or simple analgesia (n=20) iii. Physiotherapy: 6 sessions, max 18week period; exercise and manual therapy (n=22)	Oxford Shoulder score (12-60) * # Patient perception of outcome (better) (3point scale) *Insufficient data* *6, 18, 52 weeks*
Ekeberg (2009)	12/13	Clinical diagnosis of RC disease >3months: Pain on abduction, <50% reduced glenohumeral motion in no more than 1 direction, positive impingement signs; Exclusion: acromioclavicular or glenohumeral arthritis, cervical/ organ referral, generalised pain syndrome, arthritis, diabetes, fractures, surgery, medication contraindication, corticosteroids in last month, SPADI <30	i. 2ml Triamcinolone 10mg/ml + 5ml Lidocaine Hydrochloride 10mg/ml ultrasound-guided subacromial injection + 4ml Lidocaine Hydrochloride 10mg/ml Intramusclar (buttock) injection (n=53) ii. 5ml Lidocaine Hydrochloride 10mg/ml ultrasound-guided subacromial injection + 2ml Triamcinolone 10mg/ml + 2ml Lidocaine 10mg/ml intramuscular injection (n=53); Co-intervention: Physiotherapy continued if attending at baseline	Pain during activity NRS (0-9) *Insufficient data* Shoulder Pain and Disability Index (SPADI) (/100) † Adverse events *2 weeks*
Hay (2003)	10/13	Clinical diagnosis of unilateral shoulder pain (new episode), exacerbated by active/ passive shoulder movement; Exclusion: inflammatory disorder, gross structural or neurological abnormality, medication contraindication, red flags, RC rupture, fracture, surgery, physical therapy previous 1year, pregnancy; Mean day pain NRS 5.1/9	i. 40mg Methylprednisolone + 4ml Lidocaine, 1-2 subacromial injections (n=104) ii. Physiotherapy: 8x20minute sessions over 6weeks, active shoulder exercise,± ultrasound/ manual therapy (n=103)	Day pain NRS (0-9) † # Shoulder Disability Questionnaire *# Global improvement (completely recovered) (5 point scale) *6, 26 weeks*
Karthik-eyan (2010)	11/13	Clinical + X-Ray diagnosis of subacromial impingment >3months: Pain at shoulder worse with overhead activity, arc pain, tenderness, positive Hawkins-Kennedy impingement sign; positive Neers injection test; Exclusion: other pathology eg arthritis, adhesive capsulitis, major tear, injection previous 6mths, regular NSAIDS or steroids or medication contraindicated, legal proceedings, pregnant/breastfeeding	i. 40mg Methylprednisolone + 5ml 1% Lignocaine injection (n=27) ii. 20mg NSAID Tenoxicam +5ml 1% Lignocaine injection (n=31) Single subacromial anterolateral injection Co-intervention: Standardised outpatient physiotherapy	Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire (/100) * Global assessment (much better or slightly better) (5pt scale) Adverse events *4 weeks*
McInerney (2003)	10/13	Post traumatic shoulder impingement, age >16years, painful arc, pain on resisted abduction, normal radiographs, full abduction power, positive Neers injection test; Exclusion: Complete RC tear, acromioclavicular tenderness, chronic shoulder disease, shoulder crepitis, loss of external rotation, diabetes, anti-coagulated	i. 40mg Methylprednisolone + 2ml 0.5% Bupivacaine, single subacromial injection. Neers injection test prior: 8ml 0.5% Bupivicaine (n=54) ii. Neers injection test: 8ml 0.5% Bupivicaine (n=44) Co-intervention: Pendular, wall climb exercises	Pain VAS (0-10): *Insufficient data* Adverse events

	PEDro	Population Characteristics	Interventions (number randomised)	Outcome Measures/*Timepoints*
Petri (1987)	11/13	Shoulder Pain with at least 2 of: painful abduction, painful arc or tenderness to palpation supraspinatus tendon; positive Lidocaine injection test; Exclusion: bicipital tendinitis, tears (roentgnogram); frozen shoulder; arthritis, injection previous 3months	i. 1cc 40mg/ml Triamcinolone + 3cc 1% Lidocaine + Placebo tablets (n=25) ii. 1cc 40mg/ml Triamcinolone + 3cc 1% Lidocaine + 500mg Naproxen (n=25) iii. 4cc 1% Lidocaine + Naproxen 500mg (n=25) iv. 4cc 1% Lidocaine + Placebo tablets (n=25) Single injection, Tablets 2/day for 30 days Co-intervention: Range of motion exercise, heat/cold	Pain VAS (0-5) * Limitation of function VAS (0-5) * Adverse events *4 weeks*
Vecchio (1993)	9/13	Clinical diagnosis of acute RC tendinitis: pain with resisted shoulder movement, passive motion normal; Exclusion: frozen shoulder, bicipital tendinitis, acromioclavicular arthritis, RC tears, local infection, previous steroid injection	i. 1ml of 40mg/ml Methylprednisolone + 1ml 1% Lignocaine (n=28) ii. 1ml 1% Lignocaine (n=25); Single subacromial injection; Co-intervention: pendular/ wall climb home exercise	Combined day/night pain VAS: *Insufficient data* Adverse events *12 weeks*
White (1986)	7/13	Acute RC tendinitis (<12weeks): painful arc, positive Lidocaine injection test; Exclusion: calcific tendinitis, frozen shoulder, systemic inflammatory or acromioclavicular arthritis, biceps tendinitis, major RC tear, injection previous 6months; Mean Day Pain VAS 6/9	i. 1ml of 40mg/ml Triamcinalone Acetonide + Placebo tablets (n=15) ii. 1cc saline injection + 25mg oral Indomethacin (n=15); 1-2 injections, 3week interval, tablets 4x/day, Subacromial injection of 3ml 1% Lidocaine 10minutes prior. Co-intervention: Physical Therapy Pendular, wall climb, slow abduction home exercise	Total Pain (day + night) VAS (0-18)* Adverse events *3-6 weeks*
Corticosteroid Injection for Medial Epicondylalgia				
Stahl (1997)	11/13	Clinical and radiography diagnosis of medial epicondylalgia, Exclusion: ulnar neuropathy, other upper limb conditions; Mean pain VAS 3.6/10	i. 1ml 40mg Methylprednisolone +1ml 1% Lidocaine, single injection (n=30) ii. 1ml 1% Lidocaine + 1ml Saline 0.9% (n=30) Co-intervention: NSAIDS, Physical therapy	Pain VAS (0-10) † Adverse events *6, 52 weeks*
Corticosteroid Injection for Achilles (ACH) and Patellar Tendinopathy (PT)				
Capasso (1997)	7/13	Clinical + Ultrasound diagnosis of patellar tendinopathy; Mean pain VAS after 10minute run 67/100	i. 40mg Methylprednisolone Acetate + 2.5ml 1% Lignocaine (n=39) ii. 62500units Aprotinin (Kir, Leptit) + 2.5ml 1% Lignocaine (n=38) iii. 5ml .9% Saline (n=39) 2-4 paratendinous injections, 2week intervals	Pain after 10 minute run VAS *Insufficient Data* Adverse events
Fredberg (2004)	9/13	Chronic midsubstance Achilles or patellar tendinopathy >6months, clinical + ultrasound diagnosis (stage 3A or 3B, tendon thickening >1mm); Exclusion: partial or total rupture, previous steroid treatment, infection, surgery, diabetes, inflammatory disease; Mean walking pain VAS 3.1/10	i. 0.5ml 20mg Triamcinolone (Kenalog) + 3.5ml 10mg/ml Lidocaine (n=24) ii. 3.5ml 1% Lidocaine + 0.5ml 20% Intraplipid (n=24); 2-3 ultrasound-guided injections at days 0, 7, 21; Co-intervention: stretch/ strength exercises; Cross-over of placebo group offered at 3wks if athlete did not feel improvement	Walking Pain VAS (0-10) * # Adverse events *3 weeks*
Alternative Injections for Lateral Epicondylalgia (LE)				
Akermark (1995)	11/13	Clinical diagnosis LE >3months; Exclusion: nerve entrapment, neck disorders, injection in previous 8weeks, NSAIDS previous 7days; Mean pain VAS 60/100	i. 1ml 50mg/ml Glycosaminoglycan Polysulfate, Arteparon (n=34) ii. 1ml 0.9% Saline (n=31); 5 injections, 1week intervals; Co-intervention: rest 6weeks followed by stretch/ strength exercises	Pain VAS (0-100) † Adverse events *3, 26 weeks*
Peerbooms (2010)		See Corticosteroid injections for Lateral Epicondylalgia		
Petrella (2010)	8/13	Clinical or radiographic diagnosis of LE > 3months, new referrals only; Exclusion: Previous injections or acupuncture, nerve entrapment or systemic neuromuscular disorders; Mean pain at rest VAS 8.5/10	i. Sodium Hyaluronate (1.2cc) (n= 165) ii. Saline (1.2cc) (n=166) 2 injections, 1 week interval	Pain at rest VAS (0-10) † Patient global satisfaction (Likert scale 0-5; 0=not satisfied, 5=fully satisfied) Adverse events *4, 13, 52 weeks*
Scarpone (2008)	10/13	Clinical diagnosis of LE >6months, failure with physical therapy, NSAIDS and 2 steroid injections; Exclusion: steroid injection previous 6weeks, immunocompromised; Mean resting pain NRS 4.8/10	i. 1.5ml Prolotherapy: 50% Dextrose, 5% Sodium Morrhuate, 4% Lidocaine, 0.5% Sensorcaine (n=12) ii. 1.5ml 0.9% saline (n=12); Three injections each, 4week intervals	Resting pain NRS (0-10) † Adverse events *8, 16 weeks*
Wong (2005)	12/13	Clinical diagnosis of LE >3months; Exclusion: previous injection or acupuncture, nerve entrapment, systemic neuromuscular disorders; Mean pain VAS 66/100	i. 60 units Botulinum toxin, Dysport (n=30) ii. 60 units 0.9% saline (n=30) Single injection 1cm from lateral epicondyle	Pain VAS (0-100) † Adverse events *4 weeks*
Zeisig (2008)	12/13	Clinical diagnosis of chronic LE (>3months); Exclusion: interventions previous 3months, arthritis, synovitis, radiculopathy; Mean pain VAS 69/100	i. 0.5ml Polidocanol 10mg/ml (n=18) ii. 0.5ml Lidocaine Hydrochloride 10mg/ml + Epinephrine (n=18) 5mcg/ml; Single ultrasound- guided injection; Cross-over of control group >3months	Pain with gripping VAS (0-100) † Satisfaction with treatment (satisfied) (dichotomous scale) Adverse events *12 weeks*

	PEDro	Population Characteristics	Interventions (number randomised)	Outcome Measures/*Timepoints*
Alternative Injection for Rotator Cuff Tendinopathy (RC)				
Karthikeyan (2010)		see Corticosteroid injections for Rotator Cuff Tendinopathy		
Sengul (2008)	7/13	Shoulder impingement syndrome: Clinical + magnetic resonance imaging (MRI) diagnosis, positive subacromial injection test; Exclusion: positive drop arm test, adhesive capsulitis, calcific tendinitis, cervical spondylosis, radiculopathy, RC tear, fracture, dislocation, inflammatory disease, severe cardiac/pulmonary disease, malignancy	i. 2ml 20mg Sodium Hyaluronate, 3 subacromial injections, 1week intervals (n=25) ii. "Local Modalities" daily for 2weeks: Analgesic current 25W, 50Hz, 10mins, Ultrasound (n=25) Co-intervention: pendulum/ painfree active assisted exercises	Constant Murley Scale Pain subscore † American Shoulder and Elbow Surgeons(ASES) Function Score † Patient global assessment (much better) (4 point scale) Adverse events *5 weeks*
Alternative Injection for Achilles (ACH) and Patellar Tendinopathy (PT)				
Alfredson (2005)	9/13	Chronic midsubstance Achilles tendinopathy, Clinical + ultrasound diagnosis (neovascularisation); Exclusion: previous injection; Mean pain VAS with load 71/100	i. Polidocanol 5mg/ml (n=10) ii. Lidocaine Hydrochloride 5ml/ml + Adrenaline 5 mcg/ml (n=10); 1-2 ultrasound-guided injections, 3-6week interval Cross-over of control group > 3months	Pain with load VAS (0-100) † Patient satisfaction with treatment (satisfied) (Dichotomous) Adverse events *12 weeks*
Brown (2006)	9/13	Clinical diagnosis Achilles tendinopathy > 6weeks, Exclusion: paratendinitis, bursitis, enthesopathy, significant cardiovascular, renal or hepatic disease, Mean VISA 60.6/100	i. 3ml Aprotinin + 1ml Xylocaine 1% plain (n=15) ii. 3ml 0.9% Saline + 1ml Xylocaine 1% plain (n=18); 3 injections, 1week intervals Co-intervention: eccentric exercise	Tenderness Pain VAS (0-10) * # VISA (0-100)* # Patient Rated Change VAS (0-10)*# Adverse events *4, 52 weeks*
Capasso (1997)		See Corticosteroid injections for Achilles and Patellar tendinopathy		
De Vos (2010)	12/13	Clinical diagnosis Achilles tendinopathy >2months, midportion, 18-70years, thickened tendon; Exclusion: other musculoskeletal or inflammatory disorder, tendon rupture, specific medications causing tendinopathy, previous eccentric exercise program or injection with platelet-rich plasma	i. Platelet-rich plasma injection (see article for preparation notes) (n=27) ii. 4ml isotonic saline (n=27) Single, blinded peritendinous injection under US guidance, 2ml 0.5% Marcain injection prior Co-intervention: Eccentric exercise program commenced 1week after injection	VISA-A * (0-100) Patient satisfaction (good or excellent) (4point scale) *6, 24 weeks*
Hoksrud (2006)	13/13	Patellar tendinopathy >3 months, clinical and US diagnosis (neovascularisation), VISA < 75/100; Exclusion: patellofemoral pain syndrome, inflammatory joint conditions; Mean VISA 54/100	i. 2ml Polidocanol 10mg/ml (n=17) ii. 2ml Lidocaine + Adrenaline 5mg/ml +5 mcg/ml (n=16); 1-3 ultrasound-guided injections, 3-5week intervals; Cross-over of control group at 4months	VISA (0-100) * # Overall Satisfaction VAS (0-10) * # Adverse events *16 weeks*
Sundqvist (1987)	7/13	Clinical diagnosis of Achilles tendinopathy; Exclusion: local injection previous 40days, systemic steroids, NSAIDS previous 7days, medication contraindication	i. 1ml 50mg/ml Glycosaminoglycan polysulfate injection + placebo tablets (n=29) ii. 1ml Saline 0.9% injection + 50mg NSAID Indomethacin tablets (n=30); 6 peritendinous injections (3/week)	Impediment to function VAS (0-10) *Insufficient data* Adverse events
Yelland (2009)	10/13	Clinical + ultrasound diagnosis of midportion Achilles tendinosis >6weeks, >18years, VISA<80/100 for participants involved in sport or VISA<70/90 for participants not involved in sport; Exclusion: previous steroid or prolotherapy injections or surgery, previous completion of >50% of Achilles eccentric exercise protocol, allergies or medical conditions limiting treatment	i. Prolotherapy (max 5ml 20% glucose, 0.1% lignocaine, 0.1% ropivacaine) (n=14); subcutaneous peritendinous injection weely for 4-12 treatments ii. Eccentric loading exercises (n=15) based on Alfredson protocol, 3 review sessions ii. Prolotherapy plus eccentric loading exercises (n=14)	VISA-A † Worst pain during the last week NRS (0-10) † Patient global impression of change (PGIC) (7point Likert scale) (very much worse to very much better) Adverse events *6 (VISA-A, NRS), 12(PGIC), 26, 52 weeks*
Willberg (2008)	10/13	Chronic Achilles tendinopathy, clinical + ultrasound diagnosis (neovascularisation); Exclusion: previous injection; Mean pain VAS during activity 66/100	i. 5mg/ml Polidocanol (n=26) ii. 10mg/ml Polidocanol (n=26) 1-3 ultrasound- guided injections, >6-8 week interval	Pain during activity VAS (0-100) † Patient Satisfication (satisfied) (dicotomous scale) Adverse events *Follow-up after 1-3 injections*

	Overall Improvement RR [95%CI]			Pain SMD [95% CI]			Function SMD [95% CI]		
	Short-term	**Intermediate**	**Long-term**	**Short-term**	**Intermediate**	**Long-term**	**Short-term**	**Intermediate**	**Long-term**
CORTICOSTEROID INJECTION FOR LATERAL EPICONDYLALGIA									
CORTICOSTEROID INJECTION vs NO INTERVENTION									
Smidt	**2.85 [1.96, 4.16]**	NA	0.84 [0.68, 1.02]	**1.50 [1.09, 1.90]**	-0.27 [-0.63, 0.09]	-0.15 [-0.51, 0.21]	**1.44 [1.04, 1.84]**	**-0.48 [-0.85, -0.12]**	**-0.36 [-0.72, -0.00]**
Bisset	**4.72 [2.55, 8.75]**	**0.55 [0.41, 0.73]**	**0.75 [0.62, 0.90]**	**1.32 [0.92, 1.72]**	**-0.54 [-0.90, -0.18]**	**-0.46 [-0.81, -0.11]**	**1.60 [1.18, 2.01]**	**-0.53 [-0.89, -0.16]**	**-0.27 [-0.62, 0.08]**
Tonks	NA	NA	NA	**1.88 [0.84, 2.92]**	NA	NA	**1.26 [0.32, 2.19]**	NA	NA
Pooled	**3.47 [2.11, 5.69]**		**0.79 [0.69, 0.90]**	**1.44 [1.17, 1.71]**	**-0.40 [-0.67, -0.14]**	**-0.31 [-0.61, -0.01]**	**1.50 [1.22, 1.77]**	**-0.51 [-0.76, -0.25]**	**-0.32 [-0.57, -0.06]**
Heterogeneity	Chi^2 1.98 p=0.16 I^2 50%		Chi^2 0.6 p=0.44 I^2 0%	$Chi^2$1.14 p=0.57 I^2 0%	Chi^2 1.09 p=0.3 I^2 8%	Chi^2 1.45 p=0.23 I^2 31%	Chi^2 0.55 p=0.76 I^2 0%	Chi^2 0.03 p=0.86 I^2 0%	Chi^2 0.12 p=0.73 I^2 0%
CORTICOSTEROID INJECTION vs NSAID									
Hay	**7.47 [2.38, 23.46]**	NA	NA	**1.02 [0.61, 1.43]**	**-0.52 [-0.92, -0.13]**	-0.19 [-0.58, 0.19]	**0.92 [0.51, 1.32]**	-0.29 [-0.68, 0.10]	-0.19 [-0.58, 0.19]
CORTICOSTEROID INJECTION vs PLACEBO INJECTION									
Saartok	0.83 [0.25, 2.76]	NA	NA	NA	NA	NA	NA	NA	NA
Price	NA	NA	NA	**0.95 [0.41, 1.50]**	-0.42 [-0.97, 0.14]	NA	NA	NA	NA
Lindenhovius	NA	NA	NA	0.25 [-0.31, 0.80]	-0.27 [-0.84, 0.30]	NA	0.14 [-0.42, 0.69]	-0.25 [-0.82, 0.32]	NA
Newcomer	NA	NA	NA	-0.06 [-0.69, 0.57]	0.57 [-0.11, 1.25]	NA	NA	NA	NA
Pooled				Significant heterogeneity	-0.07 [-0.63, 0.50]				
Heterogeneity				Chi^2 6.25 p=0.04 I^2 68%	Chi^2 5.35 p=0.07 I^2 63%				
CORTICOSTEROID INJECTION vs PHYSIOTHERAPY									
Verhaar	**2.45 [1.51, 3.98]**	NA	0.87 [0.60, 1.24]	NA	NA	NA	NA	NA	NA
Smidt	**1.96 [1.50, 2.57]**	NA	**0.77 [0.64, 0.92]**	**1.48 [1.08, 1.87]**	**-0.52 [-0.88, -0.17]**	**-0.40 [-0.76, -0.05]**	**1.20 [0.82, 1.58]**	**-0.63 [-0.99, -0.27]**	**-0.57 [-0.93, -0.22]**
Bisset	**3.18 [2.00, 5.07]**	**0.52 [0.39, 0.70]**	**0.72 [0.60, 0.87]**	**0.79 [0.43, 1.15]**	**-0.60 [-0.96, -0.24]**	**-0.56 [-0.91, -0.20]**	**1.37 [0.98, 1.76]**	**-0.65 [-1.02, -0.29]**	**-0.57 [-0.92, -0.21]**
Tonks	NA	NA	NA	**1.15 [0.17, 2.13]**	NA	NA	**1.39 [0.38, 2.41]**	NA	NA
Pooled	**2.37 [1.75, 3.21]**		**0.76 [0.67, 0.85]**	**Significant heterogeneity**	**-0.56 [-0.82, -0.31]**	**-0.48 [-0.73, -0.23]**	**1.29 [1.03, 1.55]**	**-0.64 [-0.90, -0.39]**	**-0.57 [-0.82, -0.32]**
Heterogeneity	Chi^2 3.51 p=0.17 I^2 43%		Chi^2 0.87 p=0.65 I^2 0%	Chi^2 6.35 p=0.04 I^2 68%	Chi^2 0.09 p=0.76 I^2 0%	Chi^2 0.35 p=0.56 I^2 0%	Chi^2 0.43 p=0.81 I^2 0%	Chi^2 0.01 p=0.93 I^2 0%	Chi^2 0.0 p=0.98 I^2 0%
CORTICOSTEROID INJECTION vs ORTHOTIC DEVICES - Elbow band (EB), Wrist Splint (WS)									
Haker	**EB 6.16 [1.61, 23.56]**	0.59 [0.24, 1.47]	0.81 [0.34, 1.96]	NA	NA	NA	NA	NA	NA
	WS 13.0 [1.88, 89.74]	0.50 [0.21, 1.19]	0.75 [0.32, 1.75]						
LOW (10mg) vs HIGH (20mg) DOSE CORTICOSTEROID INJECTION (SMD>0 favours low dose)									
Price	NA	24	NA	0.04 [-0.51, 0.59]	-0.06 [-0.63, 0.50]	NA	NA	NA	NA
TRIAMCINOLONE INJECTION vs HYDROCORTISONE INJECTION (SMD>0 favours Triamcinolone)									
Price	NA	NA	NA	0.45 [-0.07, 0.97]	0.21 [-0.33, 0.75]	NA	NA	NA	NA
SINGLE vs MULTIPLE CORTICOSTEROID INJECTION (RR>1 and SMD>0 favour multiple injections; RR<1 and SMD<0 favour single injections)									
Okcu	0.92 [0.74, 1.13]	NA	**0.43 [0.25, 0.75]**	**1.71 [1.06, 2.36]**	NA	**-10.11 [-12.2, -8.01]**	NA	NA	NA
CORTICOSTEROID INJECTION (CSI) vs PLATELET-RICH PLASMA (PRP) INJECTION (SMD>0 favours CSI; SMD<1 favours PRP)									
Peerbooms	NA	NA	NA	**0.44 [0.04, 0.84]**	**-0.86 [-1.27, -0.45]**	**-0.83 [-1.24, -0.42]**	**0.52 [0.12, 0.92]**	**-0.48 [-0.88, -0.08]**	**-0.69 [-1.09, -0.28]**

	Overall Improvement RR [95%CI]			Pain SMD [95% CI]			Function SMD [95% CI]		
	Short-term	**Intermediate**	**Long-term**	**Short-term**	**Intermediate**	**Long-term**	**Short-term**	**Intermediate**	**Long-term**
CORTICOSTEROID INJECTION FOR ROTATOR CUFF TENDINOPATHY									
CORTICOSTEROID INJECTION vs PLACEBO INJECTION									
Petri	NA	NA	NA	**0.65 [0.08, 1.22]**	NA	NA	0.40 [-0.16, 0.96]	NA	NA
Adebajo	NA	NA	NA	**1.07 [0.40, 1.73]**	NA	NA	**0.94 [0.29, 1.60]**	NA	NA
Alvarez	NA	NA	NA	0.47 [-0.05, 0.99]	-0.08 [-0.60, 0.43]	NA	0.41 [-0.11, 0.93]	0.01 [-0.50, 0.53]	NA
Pooled				**0.68 [0.35, 1.01]**			**0.62 [0.29, 0.95]**		
Heterogeneity				Chi^2 1.92 p=0.38 I^2 0%			Chi^2 1.58 p=0.45 I^2 0%		
CORTICOSTEROID INJECTION vs NSAID INJECTION									
Karthikeyan	**1.54 [1.02, 2.33]**	NA	NA	NA	NA	NA	**0.98 [0.42, 1.54]**	NA	NA
CORTICOSTEROID INJECTION vs NSAIDS									
Cloke	NA	NA	NA	NA	NA	NA	0.32 [-0.24, 0.87]	0.19 [-0.42, 0.79]	-0.02 [-0.71, 0.67]
CORTICOSTEROID INJECTION vs PLACEBO INJECTION + NSAIDS									
Adebajo	NA	NA	NA	0.42 [-0.21, 1.05]	NA	NA	0.00 [-0.62, 0.62]	NA	NA
Petri	NA	NA	NA	0.18 [-0.38, 0.73]	NA	NA	-0.05 [-0.60, 0.51]	NA	NA
White	NA	NA	NA	-0.17 [-0.89, 0.55]	NA	NA	NA	NA	NA
Pooled				0.17 [-0.19, 0.53]			-0.03 [-0.44, 0.39]		
Heterogeneity				Chi^2 1.46 p=0.48 I^2 0%			Chi^2 0.01 p=0.91 I^2 0%		
CORTICOSTEROID INJECTION + NSAIDS vs PLACEBO INJECTION + NSAIDS									
Petri	NA	NA	NA	0.11 [-0.44, 0.67]	NA	NA	-0.06 [-0.62, 0.49]	NA	NA
Akgyn	NA	NA	NA	0.61 [-0.10, 1.33]		NA	0.35 [-0.35, 1.05]		NA
Alvarez-Nemegyei	NA	NA	NA	-0.34 [-0.87, 0.20]	-0.21 [-0.90, 0.49]	NA	-0.21 [-0.74, 0.32]	-0.17 [-0.86, 0.53]	NA
Pooled				0.09 [-0.43, 0.60]			-0.03 [-0.36, 0.31]		
Heterogeneity				Chi^2 4.5 p=0.11 I^2 56%			Chi^2 1.6 p=0.45 I^2 0%		
CORTICOSTEROID INJECTION vs PHYSIOTHERAPY									
Hay	**3.06 [1.27, 7.39]**	0.75 [0.43, 1.32]	NA	-0.04 [-0.32, 0.24]	-0.23 [-0.51, 0.05]	NA	0.08 [-0.20, 0.36]	-0.25 [-0.53, 0.03]	NA
Cloke	NA	NA	NA	NA	NA	NA	0.12 [-0.41, 0.64]	0.35 [-0.21, 0.92]	-0.19 [-0.85, 0.48]
Pooled							0.09 [-0.16, 0.33]	-0.00 [-0.58, 0.58]	
Heterogeneity							Chi^2 0.01 p=0.91 I^2 0%	Chi^2 3.5 p=0.06 I^2 71%	
LOCAL vs SYSTEMIC CORTICOSTEROID INJECTION (SMD <1 favours systemic corticosteroid injection)									
Ekeberg	NA	NA	NA	NA	NA	NA	-0.17 [-0.55, 0.22]	NA	NA
CORTICOSTEROID INJECTION FOR MEDIAL EPICONDYLALGIA									
CORTICOSTEROID INJECTION vs PLACEBO INJECTION									
Stahl	NA	NA	NA	0.43 [-0.08, 0.94]	NA	0.10 [-0.40, 0.61]	**0.63 [0.11, 1.15]**	NA	0.10 [-0.41, 0.60]
CORTICOSTEROID INJECTION FOR ACHILLES (ACH) AND PATELLAR TENDINOPATHY (PT)									
CORTICOSTEROID INJECTION vs PLACEBO INJECTION				**ACH/PT 0.81 [0.22, 1.40]**					
Fredberg	NA	NA	NA	ACH 0.73 [-0.11, 1.56] **PT 0.91 [0.06, 1.76]**	NA	NA	NA	NA	NA

Site		Overall Improvement RR [95%CI] Unless otherwise specified^			Pain SMD [95% CI]			Function SMD [95% CI]		
		Short-term	Intermediate	Long-term	Short-term	Intermediate	Long-term	Short-term	Intermediate	Long-term
ALTERNATIVE INJECTIONS FOR TENDINOPATHY										
POLIDOCANOL vs PLACEBO INJECTION										
Zeisig	LE	0.80 [0.44, 1.45]	NA	NA	-0.20 [-0.88, 0.47]	NA	NA	NA	NA	NA
Alfredson	ACH	11.00 [0.69, 175]	NA	NA	0.84 [-0.08, 1.77]	NA	NA	NA	NA	NA
Hoksrud	PT	NA	**^SMD 1.69 [0.88, 2.5]**	NA	NA	NA	NA	NA	0.60 [-0.10, 1.30]	NA
LOW DOSE (5mg) vs HIGH DOSE (10mg) POLIDOCANOL INJECTION (RR>1 and SMD >0 favours high dose)										
Willberg	ACH	1.02 [0.88, 1.18]	NA	NA	0.03 [-0.51, 0.58]	NA	NA	NA	NA	NA
PLATELET RICH PLASMA vs PLACEBO INJECTION										
de Vos	ACH	1.00 [0.44, 2.28]	0.88 [0.57, 1.38]	NA	NA	NA	NA	0.18 [-0.35, 0.72]	0.05 [-0.48, 0.59]	NA
PLATELET RICH PLASMA vs CORTICOSTEROID INJECTION (see Corticosteroid injection)										
Peerbooms	LE									
APROTININ vs PLACEBO INJECTION										
Brown	ACH	^SMD 0.26 [-0.42, 0.95]	NA	^SMD -0.05 [-0.81, 0.72]	0.06 [-0.63, 0.74]	NA	0.00 [-0.77, 0.77]	0.05 [-0.67, 0.77]	NA	0.06 [-0.71, 0.83]
ARTEPARON vs PLACEBO INJECTION										
Akermark	LE	NA	NA	NA	0.21 [-0.30, 0.72]	0.38 [-0.13, 0.89]	NA	NA	NA	NA
SODIUM HYALURONATE vs PLACEBO INJECTION										
Petrella	LE	^SMD **1.62 [1.37, 1.87]**	^SMD **6.11 [5.59, 6.62]**	^SMD **2.59 [2.30, 2.88]**	**3.91 [3.54, 4.28]**	**2.89 [2.58, 3.20]**	**3.91 [3.55, 4.28]**			
SODIUM HYALURONATE INJECTION vs ELECTROTHERAPY										
Sengul	RC	2.25 [0.80, 6.36]	NA	NA	0.49 [-0.08, 1.05]	NA	NA	0.38 [-0.18, 0.94]	NA	NA
PROLOTHERAPY vs PLACEBO INJECTION										
Scarpone	LE	NA	NA	NA	0.27 [-0.61, 1.15]	**2.62 [1.36, 3.88]**	NA	NA	NA	NA
PROLOTHERAPY vs ECCENTRIC EXERCISE										
Yelland	ACH	1.69 [0.92, 3.12]	1.27 [0.80, 2.02]	1.00 [0.72, 1.39]						
BOTULINUM TOXIN vs PLACEBO INJECTION										
Wong	LE	NA	NA	NA	**1.23 [0.67, 1.78]**		NA	NA	NA	NA