International Centre for Allied Health Evidence

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Systematic Review of the Literature

The effectiveness of local steroid injection to the wrist for carpal tunnel syndrome

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Abbreviations

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

Abbreviation		Abbreviation	
BCTQ SSS	Boston carpal tunnel questionnaire symptom severity score	**NaCl**	Sodium chloride
CI	Confidence Interval	**NRS**	Numerical rating scale
CTS	Carpal Tunnel Syndrome	**NSAIDs**	Non-steroidal anti-inflammatory drugs
DML	Distal motor latency	**PICO**	Population, intervention, comparator, outcome
ESWT	Extracorporeal shock wave therapy	**RCT**	Randomised controlled trial
GSS	Global symptom scale	**SIGN**	Scottish Intercollegiate Guidelines Network
HCl	Hydrochloride	**SR**	Systematic review
iCAHE	International Centre for Allied Health Evidence	**US**	Ultrasound
MRI	Magnetic resonance imaging	**VAS**	Visual analogue scale

Quality Ratings			
AQ	Acceptable Quality	LQ	Low Quality
CS	Can't say	NA	Not Applicable
HQ	High Quality	R	Reject (Unacceptable Quality)
QS	Quality of Study		

EXECUTIVE SUMMARY

Objective of the Review	The objective of this systematic review is to synthesise the evidence related to the effectiveness of injection of steroid to the wrist for carpal tunnel syndrome as a form of interventional pain management. In order to review the evidence this review aims to answer the following research questions: a) What is the evidence for the effectiveness of steroid injections into the wrist for carpal tunnel syndrome for relieving pain and/or improving functional outcomes? b) What is the evidence for the safety of steroid injections into the wrist for carpal tunnel syndrome?
Evidence sourced	The search yielded 1195 articles. After scrutiny, 1168 articles were excluded as duplicates or for failing to meet the inclusion criteria (shown in Figure 1), leaving 27 studies for inclusion in this review including 6 systematic reviews (SRs) and 21 randomised controlled trials (RCTs).
What is the evidence for the effectiveness of steroid injections into the wrist in relieving pain and/or in improving functional outcomes in patients with carpal tunnel syndrome?	• **Local steroid injection appears to be effective in the short term (approximately ≤12 weeks) in reducing pain and increasing function** (Level A recommendation based on 1x AQ SR with level 1++ evidence, 1 x HQ SR with level 1+ evidence and 1 x LQ SR with Level 1 evidence) • **Efficacy of local steroid injection appears to be reduced over time** (Level A recommendation based on 1x AQ SR with level 1++ evidence, 1 x HQ SR with level 1+ evidence and 1 x LQ SR with Level 1 evidence) • **In the long term decompression surgery appears to be more effective than local steroid injection** (Level A recommendation based on 1 x HQ SR with level 1 evidence)
What is the evidence for the safety of steroid injections into the wrist for carpal tunnel syndrome	• **Local steroid injection appears to be safe for the majority of patients (particularly if ultrasound guidance is used). However, due to swelling there is a higher risk of median nerve injury** (Level C recommendation based on 1x LQ SR with level 1- evidence)
What is the evidence for differences in effectiveness if imaging is used?	• **Ultrasound guidance should be considered as it appears to increase efficacy and safety** (Level A recommendation based on 1x AQ SR with level 1++ evidence)
Does the evidence report any information about cost effectiveness?	• **There is limited evidence that surgery, rather than nonsurgical care including steroid injections, should be considered as the initial form of treatment when patients are diagnosed with CTS that is confirmed by nerve conduction studies, as this provides symptom resolution with a favourable cost analysis** (Level D Recommendation based on one retrospective cohort study)

1. Background

1.1 Objective of this Review

The objective of this review is to synthesise the evidence related to the effectiveness of local steroid injection into the wrist for carpal tunnel syndrome as an interventional pain management technique. This review will carry out a systematic review of the best available research evidence.

This review aims to answer the following research questions:

a) What is the evidence for the effectiveness of local steroid injection to the wrist in relieving pain in people with carpal tunnel syndrome?
b) What is the evidence for the effectiveness of local steroid injection to the wrist in improving functional outcomes in people with carpal tunnel syndrome?
c) What is the evidence for the safety and risks of local steroid injection to the wrist in people with carpal tunnel syndrome?

1.2 Description of the Intervention

Carpal tunnel syndrome (CTS) is the clinical manifestation of median nerve compression within the carpal tunnel (Sternbach 1999), the space between the carpal bones and the flexor retinaculum (a fibrous band that closes the carpal tunnel) of the wrist. The compression of the median nerve occurs when there is increased intra-tunnel pressure, which can be caused by a number of factors such as trauma, inflammation and obesity (Gelberman et al. 1981; Spinner, Bachman & Amadio 1989). It is suggested that CTS is associated with certain diseases and conditions such as diabetes, hypothyroidism, pregnancy, rheumatoid arthritis, and work related factors such as repetitive upper limb activities (Maghsoudipour et al. 2008). Symptoms of carpal tunnel syndrome can include pain, burning, tingling or paraesthesia into the hand in the distribution of the median nerve (Spinner, Bachman & Amadio 1989).

There are a number of management options for carpal tunnel syndrome including decompression surgery, non-steroidal anti-inflammatory drugs (NSAIDs), oral corticosteroids, local steroid injection to the flexor retinaculum and splinting. This review specifically investigated the effectiveness of local steroid injection.

Local steroid injection may reduce tendon swelling, which may lead to decompression of the median nerve. This technique includes the injection of steroids such as methylprednisolone and betamethasone directly into the carpal tunnel usually above the carpal tunnel, near the flexor crease and just ulnar to the palmaris longus tendon (or ulnar to the midline if no palmaris longus tendon is present) (Tallia & Cardone 2003).

Steroids - Rationale

Locally, corticosteroids act to inhibit the inflammatory response induced by mechanical, chemical, or immunologic agents. This inhibition occurs in specific leukocyte functions, including leukocyte aggregation at inflammatory sites, prevention of degranulation of granulocytes, mast cells, and macrophages, and stabilization of lysosomal and other membranes (Di Rosa et al. 1986). Corticosteroids also inhibit PLA2 activity, therefore interrupting the arachidonic acid cascade. It has also been shown that local application of cortisone blocks transmission in normal nociceptive C-fibres, potentially blocking nociceptive nerves in the manner of local anaesthetics.

2. Methods

2.1 Review question

What is the evidence for the effectiveness of local steroid injection to the wrist in the treatment of carpal tunnel syndrome?

2.2 Methods

A systematic review of published research literature was undertaken to provide a synthesis of the currently available research evidence related to the effectiveness of local steroid injection to the wrist as a form of interventional pain management. A systematic and rigorous search strategy was developed to locate all published and accessible research evidence. The evidence base for this review included research evidence from existing systematic reviews, meta-analyses, and high-level primary research (RCTs, prospective cohort studies). Where no systematic reviews, RCTs, or prospective cohort studies were located, then other primary study designs (excluding commentary /expert opinion) were considered.

2.3 Search strategy

The search was developed using a standard PICO structure (shown in Table 1). Only articles published in English, using human participants and accessible in full text were included.

Table 1: Criteria for considering studies in the review

Population	People with carpal tunnel syndrome
Intervention	Local steroid injection into the carpal tunnel as a form of interventional pain management
Comparator	Any active treatment or placebo
Outcomes	• Pain-related primary outcome • Functional outcomes (range of motion, reduction of disability, return to work, quality of life) • Safety and risk • Relationship to imaging • Best practice recommendations • Cost effectiveness

A combination of search terms (shown in Table 2) was used to identify and retrieve articles in the following databases:

- OVID
  - EMBASE
  - MEDLINE
  - AMED
- ICONDA
- CINAHL
- PubMed
- Pre-Medline
- The Cochrane Library
- Scopus
- TRIP database

Table 2: Search terms for the review

Search term 1	Search terms 2	Search terms 3	Search terms 4
• Pain	• Injection	• Carpal tunnel syndrome • Wrist • Median nerve • Flexor retinaculum • Compression • Entrapment • Neuropathy	• Steroid • Betamethasone • Dexamethasone • Fluocortolone • Methylprednisolone • Paramethasone • Prednisolone • Prednisone • Triamcinolone • Hydrocortisone • Cortisone • Methandrostenolone • Stanozolol • Methenolone • Oxymetholone • Oxandrolone • Nandrolone • Diflucortolone • Fluprednisolone

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

2.4 Study Selection

Inclusion criteria

- Study types: systematic reviews, all primary research designs (randomised controlled trials (RCTs), cohort studies (prospective or retrospective)), case studies, case series
- Participants: patients with carpal tunnel syndrome
- Intervention: local steroid injection into the carpal tunnel
- Controls: any active treatment or placebo, or no intervention control
- Outcomes: pain relief (primary) functional outcomes, safety, and risk (secondary)
- Publication criteria: English language, full text available, in peer reviewed journal

Exclusion criteria

- Studies only available in abstract form, e.g. conference presentations
- Grey literature and non-English language material
- Studies involving healthy volunteers or experimentally induced pain
- Studies on interventions involving other pathologies, i.e. not carpal tunnel syndrome

2.5 Critical Appraisal

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

2.6 Data Extraction

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

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

For this review the studies that met the inclusion criteria were assessed for internal validity using the SIGN checklist for the relevant study design. Each study was graded for overall methodological quality using the SIGN levels of evidence model.

2.7 Data Synthesis

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

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

Table 3 : Modified SIGN Evidence Grading Matrix

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

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

a) Combination of data via meta-analysis
b) Quality of systematic review/trials
c) Number of RCTs
d) Consistency of the evidence

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

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

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

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

2.8 Grade of Recommendations

Recommendations will be graded according to the Scottish Intercollegiate Guidelines Network (SIGN) Grades of Recommendations (Table 4).

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

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

3. Results

3.1 Evidence Sources

The search yielded 1195 articles; following removal of duplicates 926 articles were identified for screening of title and abstract. After scrutiny, a further 862 articles were excluded for failing to meet the inclusion criteria (shown in Figure 1), leaving 64 studies for inclusion in this review. Figure 1 illustrates the process involved in study selection.

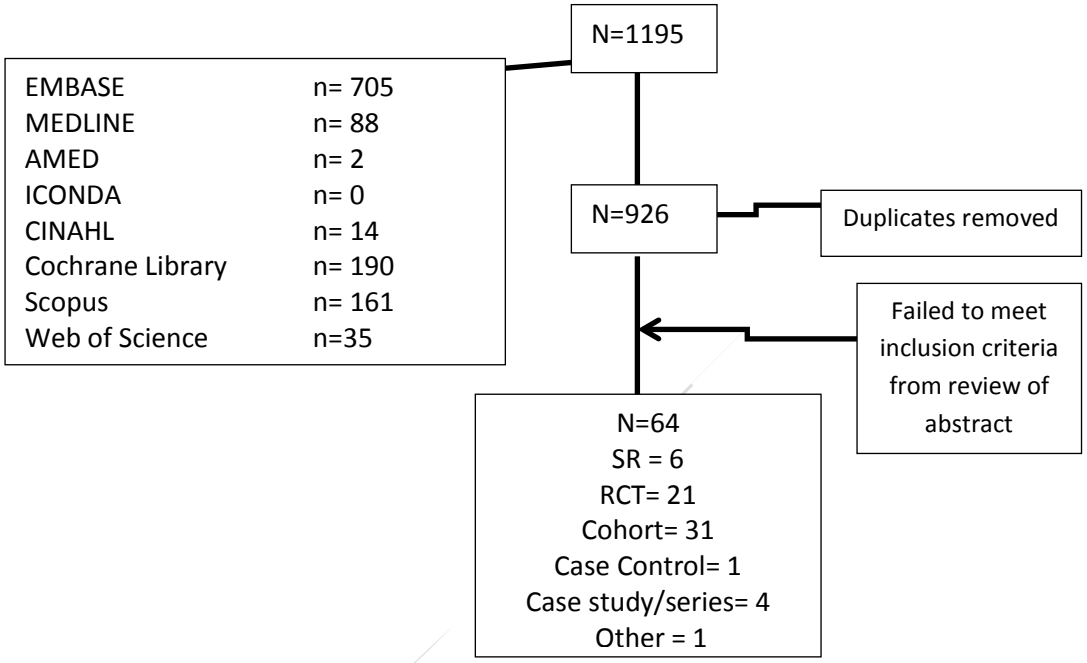

Figure 1: Flow chart of search results

As a reasonable number of high level studies including six SRs and 21 RCTs were located, it was deemed that lower levels of evidence including cohort, case control, case and retrospective studies were not required and they were therefore excluded from this review.

3.2 Quality of the Evidence

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

	N=	HQ(++)	AQ(+)	LQ(-)	R(0)
Systematic reviews	6	2	2	2	0
RCTs	21	6	10	4	1

The critical appraisal scores for each study in this review are presented in Appendix 2.

3.3 Findings

A total of six systematic reviews were located, of which four investigated the effectiveness of local steroid injection for the treatment of carpal tunnel syndrome (CTS). One investigated the most appropriate injection techniques and one investigated the safety and risks of local steroid injection for carpal tunnel syndrome. An additional 21 randomised controlled trials (RCTs) were located (i.e. which were not included in the systematic reviews) investigating predominantly short term (< 6 weeks) efficacy (n=15), long term efficacy (n=3) and appropriate injection techniques (n=3). Full details of individual studies can be found in Appendix 4 (full data extraction). Due to the large volume (systematic reviews n=6, RCTs n=21) of high level evidence, lower level studies were excluded from this review.

3.4 Outcome Measures – Pain and Function

Systematic Reviews

Pre-2005

Gerritsen et al. (2002) systematically reviewed the literature on conservative treatment options for carpal tunnel syndrome (CTS) including steroid injections, ultrasound treatment, pyridoxine and non-steroidal anti-inflammatories. The authors located three RCTs, two high quality (Dammers et al. 1999; Özdogan & Yazici 1988) and one low quality (Girlanda et al. 1993), that investigated steroid injections. The studies found limited evidence that a steroid injection proximal to the carpal tunnel or intramuscular steroid injection was more effective than placebo in improving CTS symptoms in the short-term (one month).

Study	QS	Conclusions	Level of Evidence
Gerritsen et al (2002)	AQ (+)	• There is limited evidence that steroid injections are effective	1-

Goodyear-Smith & Arroll (2004) systematically reviewed the literature to produce evidence-based recommendations for non-surgical management of CTS. The authors assessed one systematic review (Marshall et al 2002) and four RCTs (Dammers et al. 1993; Elbaz et al. 1993; O'Gradaigh & Merry 2000; Ozdogan & Yazici 1984) investigating conservative management of carpal tunnel syndrome using corticosteroids. They found strong evidence for the effectiveness of local corticosteroid injections, and to some extent oral corticosteroids, in the short-term. They concluded that for those unable or unwilling to undergo surgery, conservative modalities such as local corticosteroid injections can be tried. However, they warned that surgery may still be necessary in the future to avoid permanent nerve damage.

Study	QS	Conclusions	Level of Evidence
Goodyear-Smith & Arroll (2004)	LQ (-)	• Strong evidence that local corticosteroid injections are effective in the short term. • If conservative management is ineffective, surgery should be considered in order to prevent long term nerve damage.	1

Post-2005

Marshall et al. (2007) presented a Cochrane review of the literature to evaluate the effectiveness of local corticosteroid injection for the treatment of CTS compared to placebo injection or other conservative management interventions. The authors included 12 RCTs (Dammers et al. 1999; Armstrong et al. 2004; Ozdogan et al. 1984; Wong et al. 2001; Celiker et al. 2002; Lucantoni et al. 1992; O'Gradaigh et al. 2000; Habib et al. 2006; Wong et al. 2005; Sevim et al. 2004; Gokoglu et al. 2005; Aygul et al. 2005) with a total of 671 participants, and reported that local corticosteroid injection for CTS provided greater clinical improvement in symptoms one month after injection compared to placebo and oral corticosteroids. Significant symptom relief beyond one month was not found, with no significant differences in improvements when comparing local corticosteroid injections to NSAIDs and splinting after eight weeks or Helium-Neon laser treatment after 6 months. Additional injections (2 or more) did not appear to provide any further benefit.

Study	QS	Conclusions	Level of Evidence
Marshall et al (2007)	HQ (++)	• Steroid injection is effective in the short term. • All interventions improved clinical outcomes, and there was no statistically significant difference between injected steroids, non-steroidal anti-inflammatory drugs, or laser treatment.	1+

Verdago et al. (2008) compared the efficacy of surgical CTS treatment to non-surgical treatments including corticosteroid injection. A total of four studies met the inclusion criteria, of which two investigated efficacy of local steroid injection (Ly Pen et al. 2005; Hui et al. 2005). The authors concluded that surgical treatment was likely better than splinting, but whether it was better than steroid injection remained unclear. Further research was required for people with mild symptoms.

Study	QS	Conclusions	Level of Evidence
Verdago et al (2008)	HQ (++)	• It is unclear whether local steroid injection is as effective as surgery in the treatment of carpal tunnel syndrome.	1

Randomised Controlled Trials

Hui et al. (2004) investigated the long term (19 months) effects of oral versus injected corticosteroids in the treatment of carpal tunnel syndrome. 30 patients were treated with a single methylprednisolone injection while another 30 participants received a 10-day course of prednisolone. Authors concluded that there was no significant difference in symptoms or the proportion of patients who progressed to decompressive surgery. Few patients who did not progress to surgery (11.4%) remained asymptomatic. Patients should be informed that in most cases corticosteroids are effective in the short term, but that symptoms may reoccur.

Study	QS	Conclusions
Hui et al (2004)	LQ (-)	• There was no difference between oral and injected corticosteroids long term (19 months). • A large proportion of people still went on to receive decompression surgery in the long term.

Dammers et al. (2006) investigated the effects of three different doses of methylprednisolone injection for the treatment of CTS. Participants were randomised to receive either 20mg (n=45), 40mg (n=43) or 60mg (n=44). In the 20, 40 and 60mg groups, respectively 56%, 53% and 73% of the patients were free of important symptoms at six months follow-up. The authors concluded that a single local injection of methylprednisolone resulted in long lasting improvement with a trend in favour of the highest dose.

Study	QS	Conclusions
Dammers et al (2006)	AQ (+)	• Local steroid injections reduced the symptoms of CTS in the long term. • All doses were effective. Whilst there was no statistically significant difference between the three doses of methylprednisolone, there was a trend in favour of the higher dose.

Bardak et al. (2009) compared the effectiveness of standard conservative treatment (corticosteroid injection + splinting), tendon and nerve gliding exercises alone, and standard conservative treatment combined with tendon and nerve gliding exercises. The authors randomised 111 participants to one of three study arms: standard conservative treatment (n=41); standard conservative treatment combined with tendon and nerve gliding exercises (n=35); or tendon and nerve gliding exercise only (n=35). They concluded that conservative treatment was clinically effective. Adding tendon and nerve gliding exercises was beneficial to the management of long term CTS, but tendon and nerve gliding exercises alone were inferior to other modalities.

Study	QS	Conclusions
Bardak et al (2009)	HQ (++)	• Standard conservative treatment (corticosteroid injection + splinting) and conservative treatment combined with tendon and nerve gliding exercises were effective. • Tendon and nerve gliding exercises alone is inferior to standard conservative treatment.

Dewi et al. (2009) investigated the effectiveness of oral steroids compared to injected steroids for the treatment of CTS. The authors randomised 50 participants to either oral triamcinolone + NaCl 0.9% injection (placebo) or triamcinolone + oral placebo (active). They found that injected steroid was more effective than oral steroid two weeks after the intervention. However, in cases where patients refuse injections, they noted that oral administration could be considered as an alternative.

Study	QS	Conclusions
Dewi et al (2009)	HQ (++)	• Both oral and injected steroids are effective in reducing symptoms of carpal tunnel syndrome. • The injected steroid was found to be more effective than the oral steroid after two weeks.

Gurcay et al. (2009) compared the efficacy of local corticosteroid injection versus non-steroidal anti-inflammatory drugs (NSAIDs) in the treatment of CTS. The authors randomised 32 participants to receive either local corticosteroid injection or NSAIDs. They concluded that both groups improved, with neither intervention found to be superior to the other. Local steroid injection and NSAIDs with concomitant use of wrist splints may offer patients with CTS variable and effective treatment options for the management of functional scores and nerve conduction parameters.

Study	QS	Conclusions
Gurcay et al (2009)	AQ (+)	• Both corticosteroid injection and NSAIDs are effective in relieving symptoms of carpal tunnel syndrome.

Bilgici et al. (2010) compared the efficacy of ultrasound therapy and local corticosteroid injection plus splinting on symptoms and nerve conduction tests in people with CTS. The authors randomised 49 hands of 34 patients to ultrasound (n=16) or steroid and splinting (n=18). They concluded that both ultrasound therapy and corticosteroid injection plus splinting were effective for the clinical symptoms and electrophysiological findings of CTS. Thus, ultrasound may be an alternative therapy, particularly in patients who do not accept injection or splinting.

Study	QS	Conclusions
Bilgici et al (2010)	HQ (++)	• Both ultrasound and corticosteroid injections plus splinting were effective in the treatment of carpal tunnel syndrome.

Raeissadat & Soltani (2010) investigated the long term (10 months) effect of laser therapy versus local corticosteroid injection. The authors randomised 65 hands to receive either laser therapy or local corticosteroid steroid injection for the treatment of CTS, but failed to report the number of participants included in each group. They concluded that low level laser therapy was as effective as local injection in reducing pain and severity of disease in patients with mild to moderate carpal tunnel syndrome after 10 months.

Study	QS	Conclusions
Raeissadat & Soltani (2010)	LQ (-)	• Low level laser therapy is as effective as local steroid injection after 10 months.

Peters-Veluthamaningal et al. (2010) investigated the effects of local corticosteroid compared to a placebo (NaCl) injection in the treatment of CTS. The authors randomised 69 participants to receive either intra-carpal injection of 1ml triamcinolonacetonide 10mg/ml or 1 ml NaCl (placebo). They concluded that corticosteroid injections for CTS provided by general practitioners were effective in the short-term when compared to placebo injections. These short-term treatment effects of steroid injections deteriorated during the 12 month follow-up period, with half of the cohort of steroid-responders reporting recurrence of symptoms.

Study	QS	Conclusions
Peters-Veluthamaningal et al (2010)	HQ (++)	• Corticosteroid injections are effective in the short term. • After 12 months the beneficial effects of corticosteroid injections deteriorated.

Karadas et al. (2011) investigated the efficacy of injections of corticosteroid (triamcinolone), anaesthetic (procaine hydrochloride (HCl)) and a combination of both. A total of 99 patients (120 CTS) were randomised into three groups. Group 1 received 40 mg of triamcinolone acetonide, group 2 received 4 ml of 1% procaine HCl, and group 3 received both 40 mg of triamcinolone acetonide and 4 ml of 1% procaine HCl. Distal motor latency, compound sensory action potential amplitude, sensory nerve conduction velocity and visual analogue pain scores improved significantly in each group two months and six months after treatment ($P<0.05$). Significant differences were not observed between groups 1 and 2 or between groups 1 and 3 with respect to electrophysiologic findings at baseline or at two or six months after treatment ($P < 0.05$). Group 3 had better compound sensory action potential amplitude and sensory nerve conduction velocity scores than group 2 at six months ($P<0.05$) and better visual analogue scores than group 2 at two or six months ($P<0.05$). The authors concluded that local anaesthetic (procaine HCl) and steroid (triamcinolone) injection effectively reduced symptoms of CTS and improved the nerve conduction results.

Study	QS	Conclusions
Karadas et al (2011)	AQ (+)	• Both steroid and anaesthetic injections were effective in the treatment of carpal tunnel syndrome. • Anaesthetic should be considered in those where steroid injection is contraindicated.

Karadas et al. (2012) investigated the effect of corticosteroid (triamcinolone) or anaesthetic (procaine HCl) injection compared to a saline control. The authors randomised 57 patients (90 median nerves) into three groups. Group 1 was injected with 1 ml 0.09% saline (placebo), group 2 was injected with 40 mg triamcinolone acetonide, and group 3 was injected with 4 ml 1% procaine HCl. Clinical and electrophysiological evaluations improved significantly in groups 2 and 3 at two and six months post treatment ($p < 0.05$), with no significant changes observed in group 1 ($p > 0.05$). There was no difference between groups 2 and 3 in terms of change scores for any outcome post-treatment ($p > 0.05$). The authors concluded that both corticosteroid and local anaesthetic injections were effective in the treatment of CTS compared to a placebo.

Study	QS	Conclusions
Karadas et al (2012)	AQ (+)	• Both steroid and anaesthetic injections were effective in the treatment of carpal tunnel syndrome when compared to a placebo.

Ly-Pen et al. (2012) investigated the long term (2 years) effects of surgical decompression and local steroid injection for the treatment of CTS. The authors followed up participants from a previous study (Ly-Pen et al. 2005) where participants were randomly assigned to either

decompression surgery or local steroid injection. They concluded that while both steroid injection and surgical decompression were effective treatments for CTS, surgery was superior 2 years after the intervention.

Study	QS	Conclusions
Ly-Pen et al (2012)	AQ (+)	• Surgery was more effective than local steroid injection 2 years after the intervention.

Atroshi et al. (2013) investigated the efficacy of first time local injection of two different doses of methylprednisolone compared to placebo up to one-year post treatment in patients with idiopathic CTS. The authors randomised a total of 111 patients to either 80mg of methylprednisolone, 40mg of methylprednisolone or placebo injection administered into the subfascia of the soft tissues of the carpal tunnel. The authors concluded that while methylprednisolone injections were effective in relieving symptoms in the short term (10 weeks) and reduced the rate of surgery after one year, three out of four patients still required surgery within one year.

Study	QS	Conclusions
Atroshi et al (2013)	HQ (++)	• Methylprednisolone is effective in relieving symptoms of CTS at 10 weeks. • Rate of surgery at 1 year was reduced by methylprednisolone injections, however 3 out of 4 participants still had surgery within 1 year of injection.

Ismatullah (2013) compared the effectiveness of local steroid injection and carpal tunnel release surgery over a 12 week period in 40 patients with CTS. The authors concluded that local steroid injection gives only transient relief in CTS, whereas carpal tunnel release surgery provides long-lasting relief.

Study	QS	Conclusions
Ismatullah (2013)	AQ (+)	• Both steroid injection and surgery were effective in the short term. • Surgical intervention was found to have longer lasting effects than steroid injection.

Seok & Kim (2013) compared extracorporeal shock wave therapy (ESWT) to local steroid injection for the management of CTS. They randomly allocated 36 patients to either one session of ESWT (1000 shots at maximal tolerable intensity) or one session of steroid injection. Both groups showed significant reductions on the visual analogue scale at one and three months post-treatment compared to baseline. For the symptom severity score on the Levine Self-assessment Questionnaire, the ESWT group showed a significant reduction at one and three months post-treatment, whereas the steroid injection group showed a significant reduction at three months post-treatment. For the nerve conduction parameters, there were mild but non-significant improvements in the ESWT group, whereas sensory nerve conduction velocity, sensory nerve action potential amplitude, and distal sensory and motor latencies of the median nerve were significantly improved in the steroid injection group. The authors concluded that, although not as effective as steroid injection, ESWT could be useful in relieving symptoms of CTS with the added benefit of being non-invasive.

Study	QS	Conclusions
Seok & Kim (2013)	AQ (+)	• Extracorporeal shock wave therapy can be useful where invasive techniques (injection and surgery) are not appropriate.

Soltani et al. (2014) compared the effectiveness of low-level laser therapy versus local steroid injection in 38 participants (50 hands) with a new episode of mild to moderate severity CTS. In the steroid group, patients were given a single local corticosteroid injection of hydrocortisone 50mg (2 ml) into the carpal tunnel. In the laser group, laser therapy was administered via a low potent laser) characterized by amplitude of 775 nm, frequency of 6500 Hz and intensity of 20 j/cm^2) at five points over 11 seconds along the median nerve passage above the carpal tunnel. Analyses showed favourable outcomes in both groups in terms of visual analogue scores and median distal motor and sensory latencies ($p<0.001$ for all comparisons). Electrophysiologic studies did not imply any significant differences in severity (Chi-squared test $p = 0.28$) or change in the grade of the disease between the two groups. In addition, eight weeks post-treatment there were no significant differences between the two groups in mean visual analogue scores (Mann-Whitney test $p = 0.45$), median motor distal latency (Mann-Whitney test $p = 0.08$) or sensory distal latency (Mann-Whitney test $p = 0.70$). The authors concluded that both local steroid injection and low-level laser therapy were effective in the short term management of carpal tunnel syndrome.

Study	QS	Conclusions
Soltani et al (2013)	HQ (++)	• Both low-level laser therapy and local steroid injection are effective in the short-term management of carpal tunnel syndrome.

Andreu et al. (2014) investigated the evolution of nerve conduction test parameters with decompression surgery compared to corticosteroid injection 12 months post-treatment. The authors randomised 163 participants to receive either decompression surgery or local corticosteroid injection. Although clinical outcome improved in a similar way in both groups, the authors found statistically significant improvement in three (distal motor latency, sensory conduction velocity and sensory amplitude) of four neurophysiologic parameters only in the surgery group when compared to baseline. They concluded that at 12 months follow up, both methods were clinically effective in reducing symptoms of CTS. However, statistically significant improvements in nerve conduction parameters were seen only in the surgery group.

Study	QS	Conclusions
Andreu et al (2014)	LQ (-)	• Both corticosteroid injections and decompressive surgery are clinically effective in reducing symptoms of CTS at 12 months follow up. • Only surgery results in an improvement of neurophysiological parameters at 12 months follow up.

Awan et al. (2015) compared the effectiveness of local steroid injection to the mini incision surgical technique in the treatment of CTS. After one month they found that the steroid injection was effective in 69.0% cases while mini incision technique was effective in 56.9% cases. The authors concluded that both techniques improved pain. However there was no statistically significant difference between the two techniques, and therefore in the short term neither technique was superior.

Study	QS	Conclusions
Awan et al (2015)	0	• Both steroid injection and surgery improved pain. • Neither technique was superior.

Bahrami (2015) investigated the short-term effects of progesterone and local corticosteroid injections in the treatment of female patients with CTS. The authors randomly assigned 60 hands with mild to moderate CTS to either corticosteroid or progesterone local injection. Ten weeks post treatment, pain severity and median nerve sensory and motor latencies decreased while patients' functional status increased meaningfully in both groups, with no differences between the two groups. Pain severity was milder and the duration of post-injection pain was shorter in the corticosteroid group. The rates of patient satisfaction were also meaningfully higher in the corticosteroid group. The authors concluded that both corticosteroid and progesterone injections were effective in short-term improvement of electrodiagnostic and clinical outcomes, with no statistical difference between the two groups.

Study	QS	Conclusions
Bahrami (2015)	AQ (+)	• Both corticosteroid and progesterone local injections were effective in the treatment of CTS. • There was no difference in improvement between corticosteroid and progesterone groups.

3.5 Overview of findings

A number of included RCTs reported the same outcome measures including pain visual analogue scale (VAS), global symptom scale (GSS), Boston carpal tunnel questionnaire symptom severity score (BCTQ SSS) and the electrophysiologic outcome distal motor latency (DML). Where possible results were combined to provide an overview of both the efficacy of local steroid injections (see figures 2-5) and efficacy of steroid injection compared to other treatment strategies such as surgery (see figures 6-9). While these figures are limited to only those papers that reported the data for the specific outcomes it appears that all outcomes showed improvement in the short term which gradually reduced over time. While local steroid injections were effective in the short term when compared to other intervention strategies, particularly decompression surgery, steroid injection was comparably effective. However, it appears that surgery is more effective in the long-term.

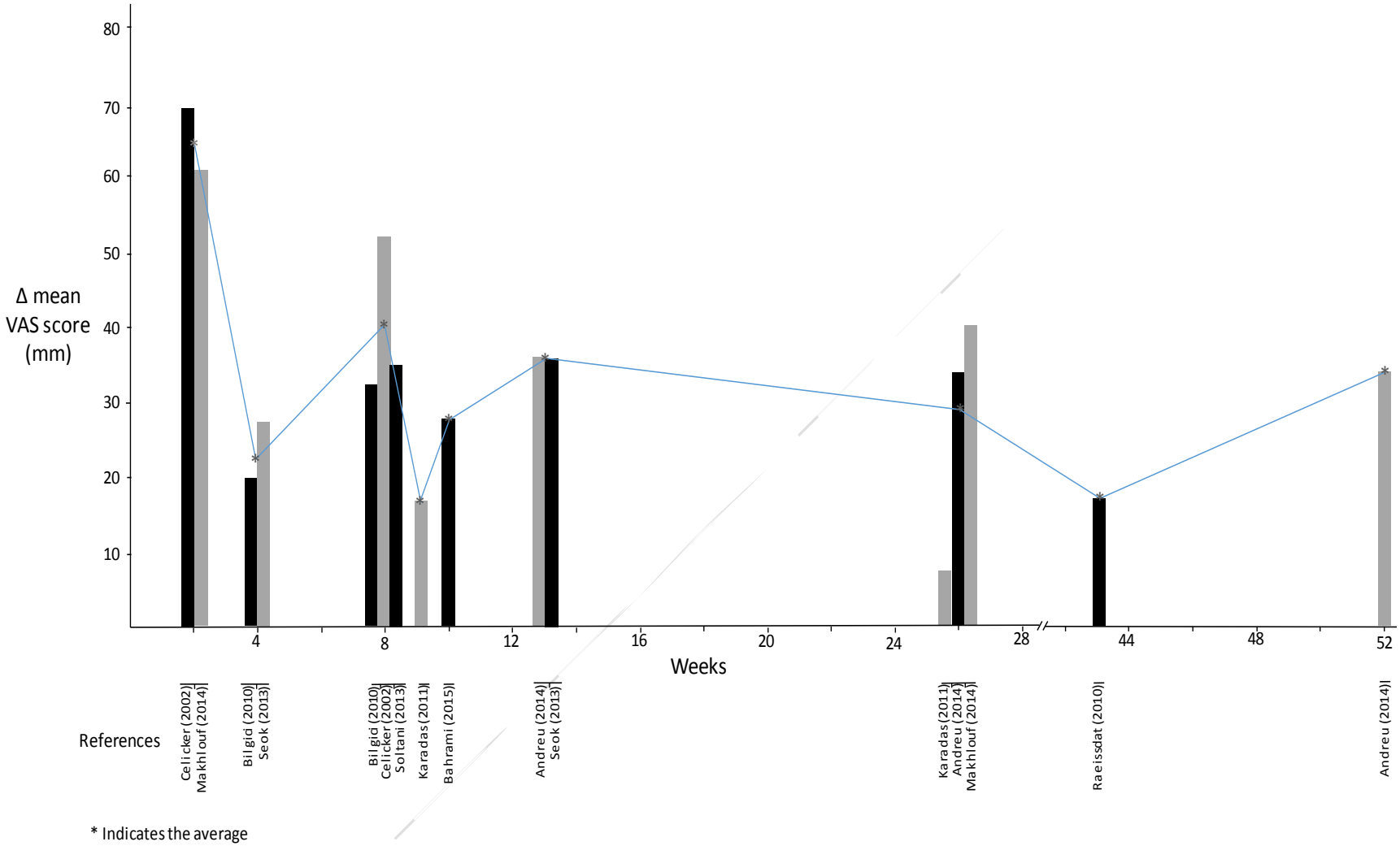

Figure 2: Mean change in pain visual analogue scale (VAS) over time for the local steroid injection group

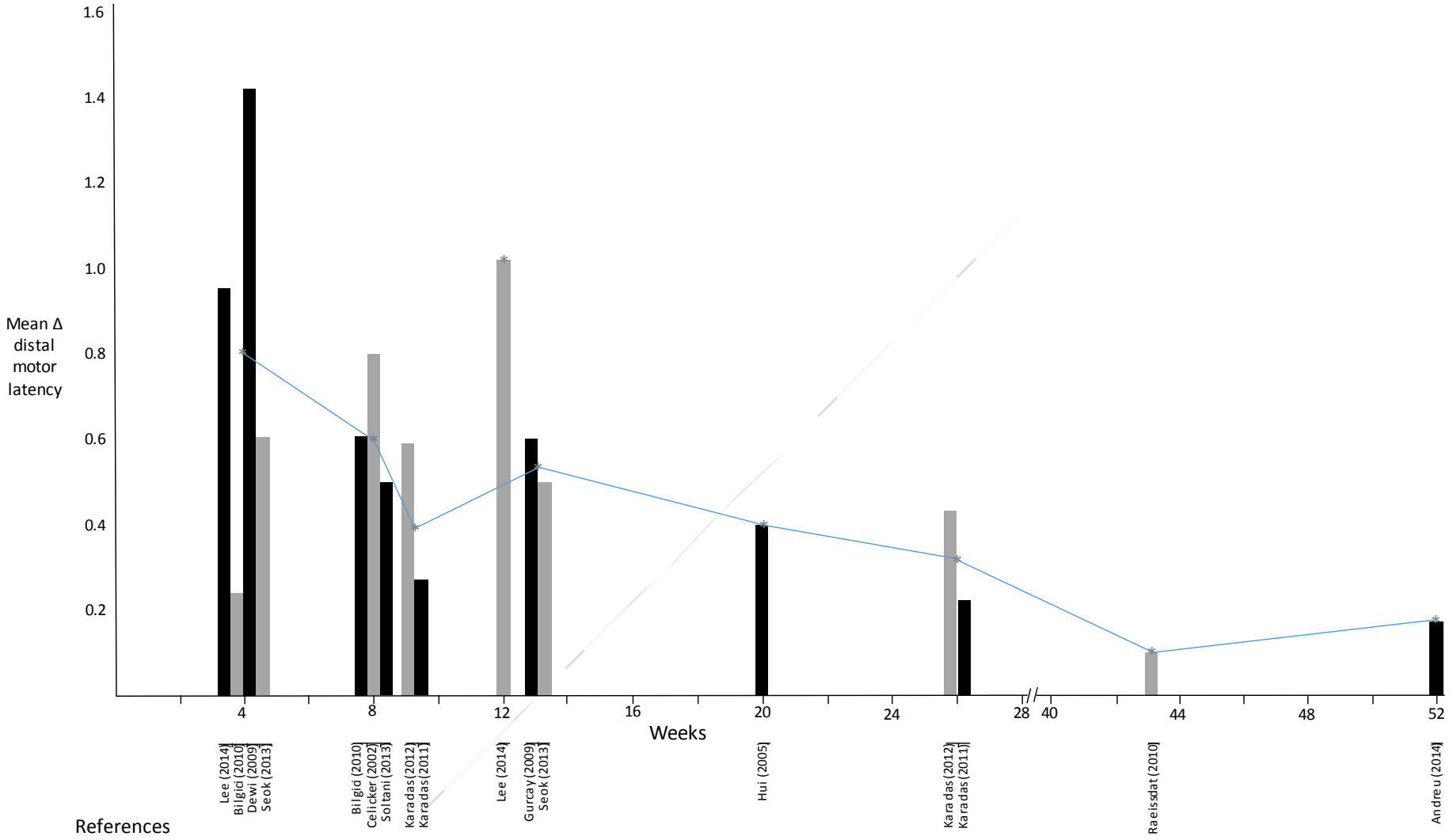

Figure 3: Mean change in distal motor latency over time for the local steroid injection group

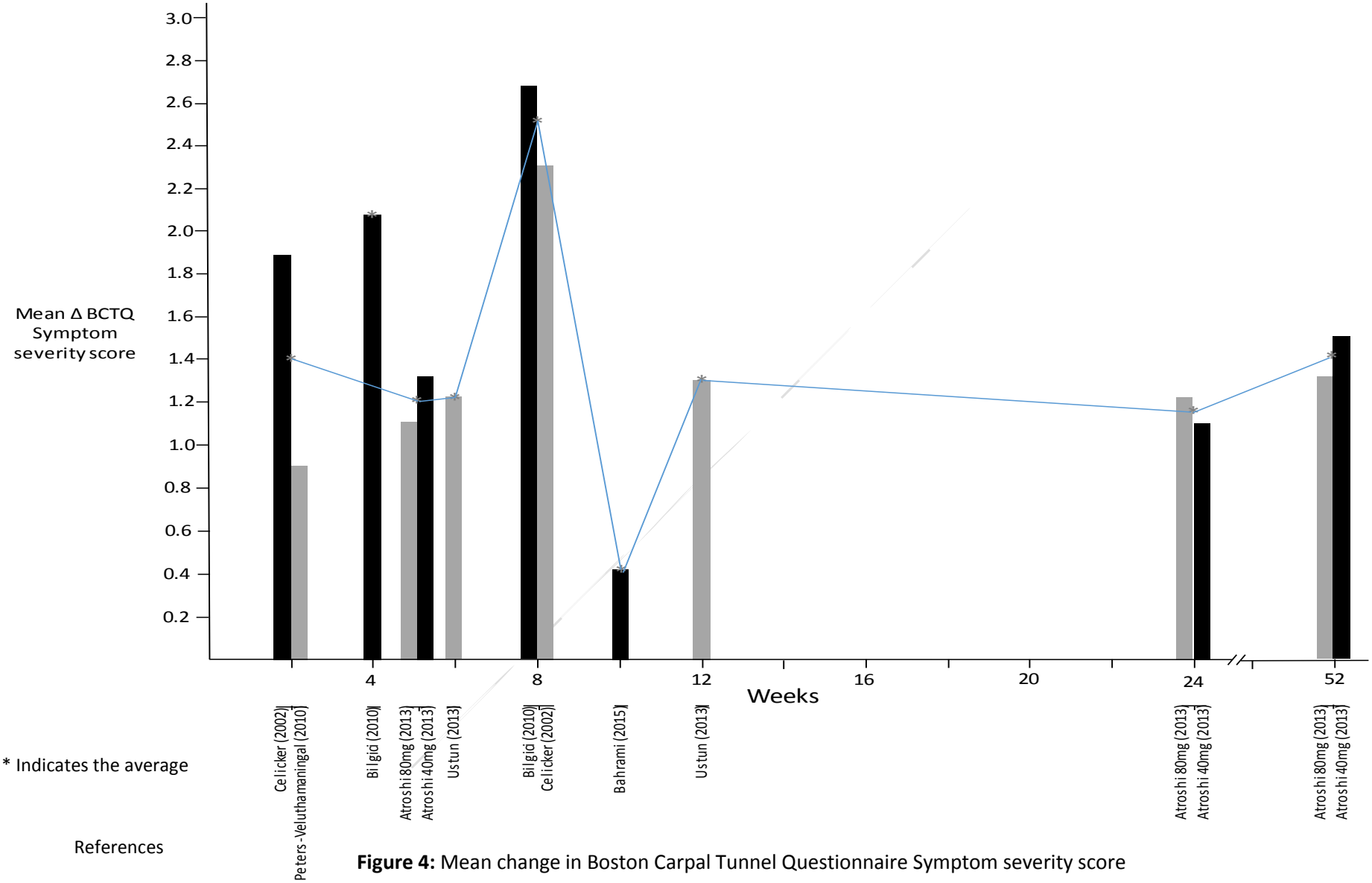

Figure 4: Mean change in Boston Carpal Tunnel Questionnaire Symptom severity score

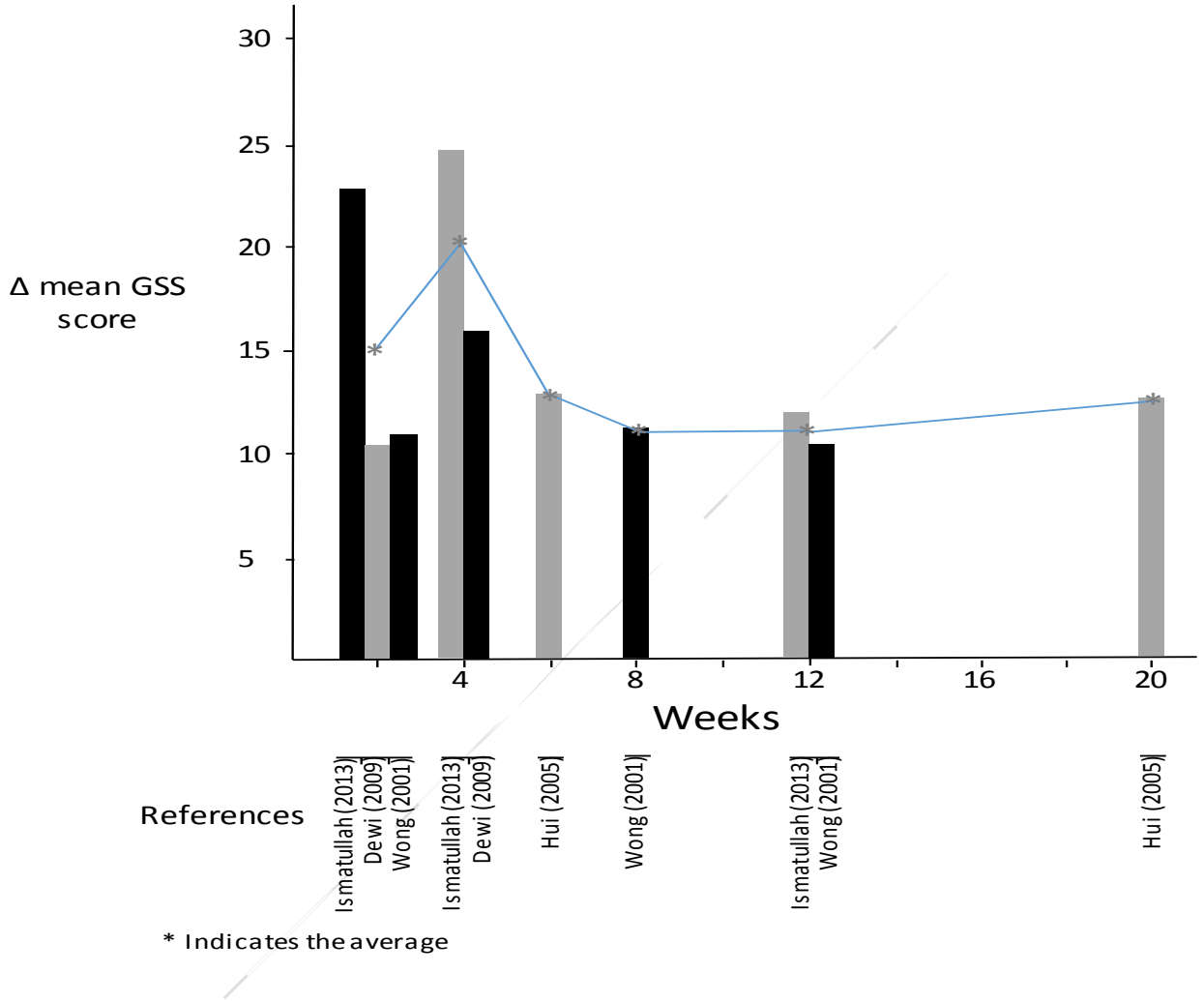

Figure 5: Mean change in global symptom score over time for the local steroid injection group

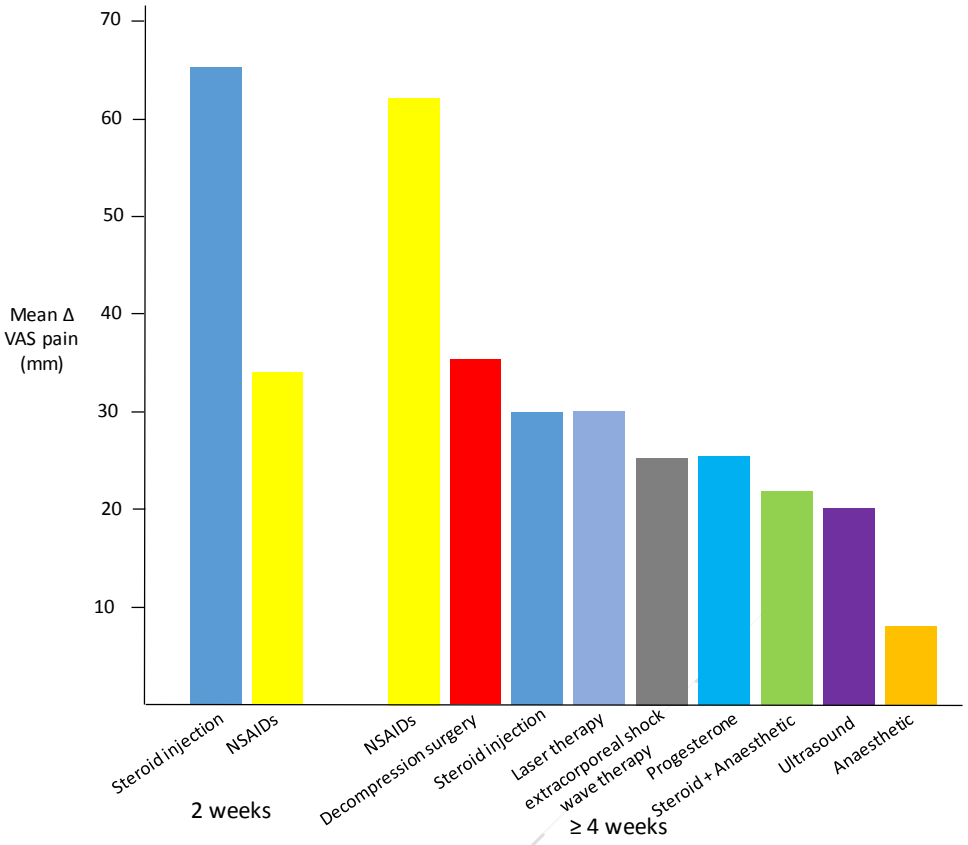

Figure 6: Steroid injection compared to other carpal tunnel treatment options

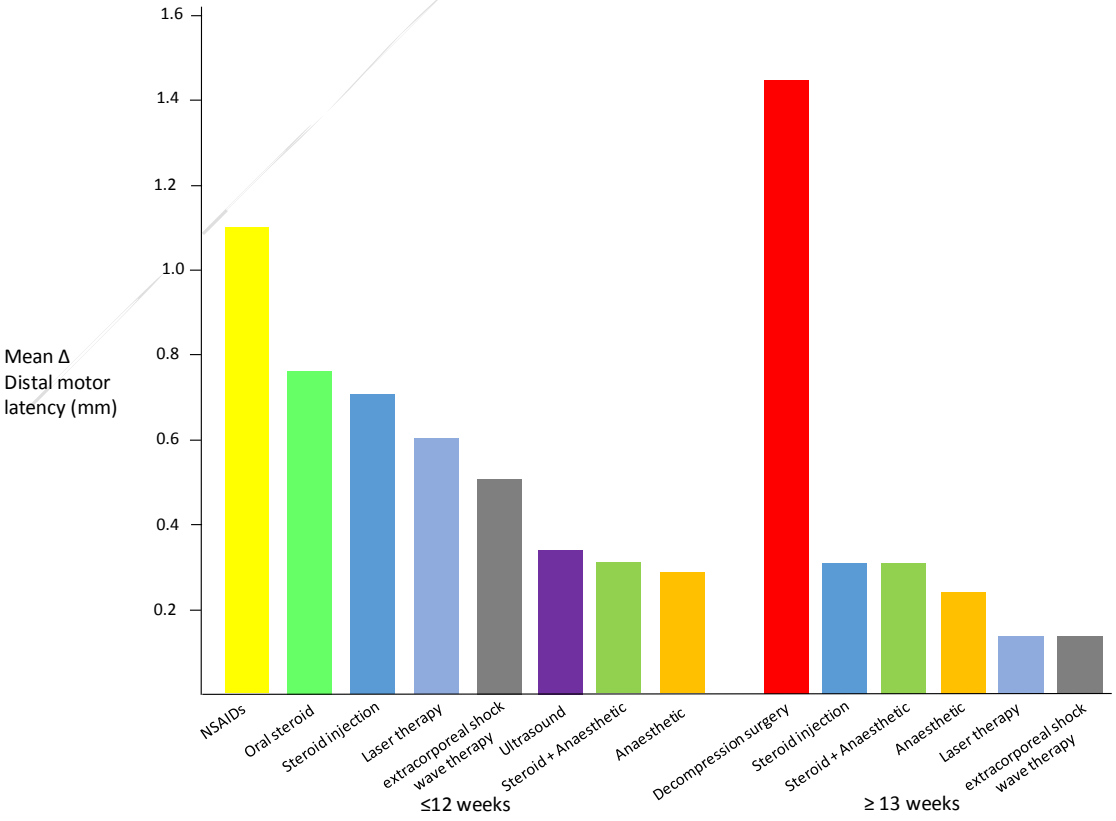

Figure 7: Steroid injection compared to other carpal tunnel treatment options

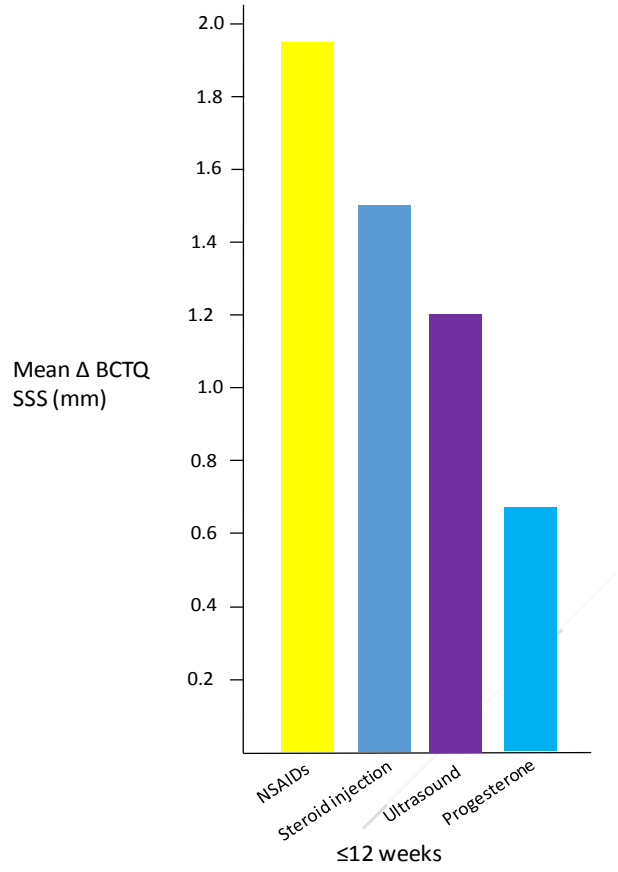

Figure 8: Steroid injection compared to other carpal tunnel treatment options

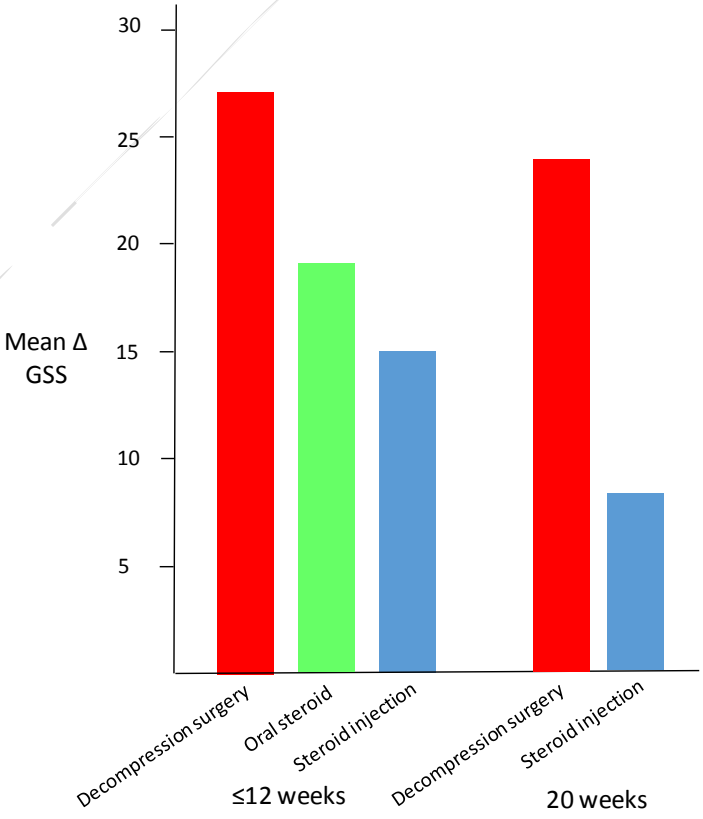

Figure 9: Steroid injection compared to other carpal tunnel treatment options

3.6 Injection technique

Systematic Reviews

Chen et al. (2015) assessed the comparative clinical effectiveness of different injection approaches for patients with CTS. A total of 10 RCTs were included in the systematic review (Habib et al. 2006; Lee et al. 2014; Üstan et al. 2015; Makhlouf et al. 2014; Peters-Veluthamaningal et al. 2010; Armstrong et al. 2004; Atroshi et al. 2013; Dammers et al. 1999; Karadas et al. 2012; O'Gradaigh and Merry 2000). The authors conducted a meta-analysis of four techniques including proximal corticosteroid injection (PI) (injection site is proximal to carpal tunnel near the flexor crease); distal corticosteroid injection (DI) (injection site is distal to the middle of the flexor crease); ultrasound-guided in-plane injection (Ulnar-I) (the needle enters the skin at the side of the transducer; the needle traverses the plane of ultrasound and the whole shaft is visualised as it progresses towards the target); and ultrasound-guided out-plane injection (Ulnar-O) (the needle enters the skin away from the transducer, and is aimed at the plane of sound, with just the needle tip visualised). The authors concluded that local corticosteroid injections were more effective than placebo at short-term follow-up, with the most effective approach being the Ulnar-I, suggesting that steroid injections for CTS should be conducted under radioscopic guidance.

Study	QS	Conclusions	Level of Evidence
Chen et a. (2015)	AQ (+)	• Local corticosteroid injections were more effective than placebo at short-term follow-up. • For injection approaches, the Ultrasound-guided in-plane injection approach might be more effective than the ultrasound-guided out-plane injection approach or blind injection.	1++

Randomised Controlled Trials

Lee et al. (2014) evaluated the efficacy of ultrasound guided (in-plane vs out-plane) injection compared to blind injection with no radiographic guidance. Both ultrasound guided techniques were more effective than blind injection, and the in-plane ultrasound guided technique was more effective than the out-plane technique. The authors concluded that ultrasound guided local steroid injection using an in-plane ulnar approach in the CTS may be more effective than out-plane or blind injection.

Study	QS	Conclusions
Lee et al (2014)	LQ (-)	• Ultrasound guided steroid injection was more effective than blind injection. • In-plane ultrasound ulnar approach was more effective than out-plane ultrasound guided approach.

Makhlouf et al. (2014) investigated the effects of local steroid injection with sonographic needle guidance on CTS symptoms and cost-effectiveness. The authors randomised 64 participants (77 carpal tunnel injections) to receive either guidance by anatomic landmark palpitation or sonographic guidance. They concluded that carpal tunnel injection performed with sonographic image guidance significantly and meaningfully reduced procedural pain,

reduced pain scores and increased cost-effectiveness in certain practice venues (hospital in- and out-patient), but increased medical costs in other settings (physician's office).

Study	QS	Conclusions
Makhlouf et al (2014)	AQ (+)	• Sonographic needle guidance is more effective than landmark palpation. • Cost effectiveness is dependent on the location of the procedure; in this study, sonographic needle guidance reduced costs in hospital settings but increased costs in the physician's office.

Üstun et al. (2013) investigated the efficacy of conducting local steroid injection for CTS under the guidance of ultrasound compared to landmark palpation (blind injection). The authors randomised 46 participants to two groups, 23 in each group. They concluded that both ultrasound guided and blind injections were effective. Earlier onset and greater symptom relief were found with the ultrasound guided technique compared to the blind technique.

Study	QS	Conclusions
Üstun et al (2013)	AQ (+)	• Both ultrasound guided and blind injection techniques are effective, however ultrasound-guided is more effective.

3.7 Safety & Risk

Kim & Park (2014) presented a narrative review of the literature on median nerve injuries caused by carpal tunnel injections. The authors found that median nerve injuries resulted from direct needle injuries, breakdown of the blood-nerve barrier, neurotoxicity of the injected steroids, and pressure effect of the steroid. Nerve injuries could occur when the needle was incorrectly placed and people with CTS were at higher risk of this occurring because the median nerve was swollen.

At the time of injection, median nerve injury may present as shooting pain with numbness, parathesia and other sensory deficits and distortion in the area supplied by the median nerve. Other reported symptoms include motor weakness, thenar atrophy, allodynia, hyperesthesia and hypoalgesia. The most appropriate management of median nerve injury is unclear. Some physicians suggest immediate surgical intervention, while others believe conservative management alone is sufficient for an incomplete nerve injury.

The authors concluded that if injections are required, appropriate needle positioning is vital to prevent nerve injury, although there may be a higher risk of injury due to swelling.

Study	QS	Conclusions	Level of Evidence
Kim & Park (2015)	0	• People with carpal tunnel syndrome may be at increased risk of median nerve injury from local steroid injection due to swelling.	1-

3.9 Economic

This review found one retrospective cohort study that compared the economic costs associated with steroid injection to surgery. Pomerance et al. (2009) reviewed the case notes of 120 patients who were divided into two groups. The first group had chosen nonsurgical

	treatment, whereas the second group had chosen surgery with no nonsurgical treatment. Patients were matched on age, gender, severity of nerve conduction abnormalities, body mass index, smoking history, job category, and insurance coverage. Steroid injections were used in 18 patients in the first group. Thirty-two patients in the first group elected to have surgery during the follow-up period. The cost of care averaged $3335 +/- $2097 in the first group and $3068 +/- $983 in the second group The authors reported that the direct cost of nonsurgical care of confirmed CTS did not show a significant difference from that of surgical treatment without preoperative splinting or therapy. The incremental cost– utility ratio for carpal tunnel surgery was favourable. The authors concluded that surgery, rather than nonsurgical care, should be considered as the initial form of treatment when patients are diagnosed with CTS that is confirmed by nerve conduction studies, as this provides symptom resolution with a favourable cost analysis.

4. Recommendations

Summary of Recommendations	• **Local steroid injection appears to be effective in the short term (approximately ≤12 weeks) in reducing pain and increasing function** (Level A recommendation based on 1x AQ SR with level 1++ evidence, 1 x HQ SR with level 1+ evidence and 1 x LQ SR with Level 1 evidence) • **Efficacy of local steroid injection appears to be reduced over time** (Level A recommendation based on 1x AQ SR with level 1++ evidence, 1 x HQ SR with level 1+ evidence and 1 x LQ SR with Level 1 evidence) • **In the long term, decompression surgery appears to be more effective than local steroid injection** (Level A recommendation based on 1 x HQ SR with level 1 evidence) • **Ultrasound guidance should be considered as it appears to increase efficacy and safety**. (Level A recommendation based on 1x AQ SR with level 1++ evidence) • **Local steroid injection appears to be safe for the majority of patients (particularly if ultrasound guidance is used); however due swelling there is a higher risk of median nerve injury** (Level C recommendation based on 1x LQ SR with level 1- evidence)

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6. Appendices

Appendix 1: SIGN Checklists

SIGN Critical Appraisal Tool for systematic reviews and Meta-analyses

SIGN	**Methodology Checklist 1: systematic reviews and Meta-analyses** SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C,. et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, **7**:10 doi:10.1186/1471-2288-7-10. Available from http://www.biomedcentral.com/1471-2288/7/10 [cited 10 Sep 2012]*
Study identification (*Include author, title, year of publication, journal title, pages*)	
Guideline topic:	Key Question No:
Before completing this checklist, consider: Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.	
Checklist completed by:	

Section 1: Internal validity

	In a well conducted systematic review:	***Does this study do it?***	
1.1	The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	Yes □ **If no reject**	No □
1.2	A comprehensive literature search is carried out.	Yes □ Not applicable □ **If no reject**	No □
1.3	At least two people should have selected studies.	Yes □	No □ Can't say □
1.4	At least two people should have extracted data.	Yes □	No □ Can't say □
1.5	The status of publication was not used as an inclusion criterion.	Yes □	No □
1.6	The excluded studies are listed.	Yes □	No □
1.7	The relevant characteristics of the included studies are provided.	Yes □	No □
1.8	The scientific quality of the included studies was assessed and reported.	Yes □	No □
1.9	Was the scientific quality of the included studies used appropriately?	Yes □	No □
1.10	Appropriate methods are used to combine the individual study findings.	Yes □ Can't say □	No □ Not applicable □

1.11	The likelihood of publication bias was assessed appropriately.	Yes □ No □ Not applicable □
1.12	Conflicts of interest are declared.	Yes □ No □
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review?	High quality (++) □ Acceptable (+) □ Low quality (-)□ Unacceptable – reject 0 □
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes □ No □
2.3	**Notes:**	

SIGN Critical Appraisal Tool for Controlled trials

Methodology Checklist 2: Controlled Trials

Study identification (*Include author, title, year of publication, journal title, pages*)

Guideline topic:	Key Question No:	Reviewer:

Before completing this checklist, consider:

1. Is the paper a **randomised controlled trial** or a **controlled clinical trial**? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a **controlled clinical trial** questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

Reason for rejection: 1. Paper not relevant to key question ☐ 2. Other reason ☐ (please specify):

SECTION 1: INTERNAL VALIDITY

In a well conducted RCT study…		***Does this study do it?***
1.1	The study addresses an appropriate and clearly focused question.	Yes ☐ No ☐ Can't say ☐
1.2	The assignment of subjects to treatment groups is randomised.	Yes ☐ No ☐ Can't say ☐
1.3	An adequate concealment method is used.	Yes ☐ No ☐ Can't say ☐
1.4	The design keeps subjects and investigators 'blind' about treatment allocation.	Yes ☐ No ☐ Can't say ☐
1.5	The treatment and control groups are similar at the start of the trial.	Yes ☐ No ☐ Can't say ☐
1.6	The only difference between groups is the treatment under investigation.	Yes ☐ No ☐ Can't say ☐
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	Yes ☐ No ☐ Can't say ☐
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).	Yes ☐ No ☐ Can't say ☐ Does not apply ☐
1.10	Where the study is carried out at more than one site, results are comparable for all sites.	Yes ☐ No ☐ Can't say ☐ Does not apply ☐

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1	How well was the study done to minimise bias? *Code as follows:*	High quality (++)☐

		Acceptable (+)☐ Low quality (-)☐ Unacceptable – reject 0 ☐
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	
2.4	**Notes.** Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.	

SIGN Critical Appraisal Tool for cohort studies

SIGN

Methodology Checklist 3: cohort studies

Study identification (*Include author, title, year of publication, journal title, pages*)		
Guideline topic:	Key Question No:	Reviewer:

Before completing this checklist, consider:

1. Is the paper really a cohort study? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist..

Reason for rejection: 1. Paper not relevant to key question ☐ 2. Other reason ☐ (please specify):

Please note that a retrospective study (ie a database or chart study) cannot be rated higher than +.

Section 1: Internal validity

	In a well conducted cohort study:	Does this study do it?	
1.1	The study addresses an appropriate and clearly focused question.[1]	Yes □ Can't say □	No □
	SELECTION OF SUBJECTS		
1.2	The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Yes □ Can't say □	No □ Does not apply □
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied.	Yes □	No □ Does not apply □
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	Yes □ Can't say □	No □ Does not apply □
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed.		
1.6	Comparison is made between full participants and those lost to follow up, by exposure status.	Yes □ Can't say □	No □ Does not apply □
	ASSESSMENT		

1.7	The outcomes are clearly defined.	Yes □ Can't say □	No □
1.8	The assessment of outcome is made blind to exposure status. If the study is retrospective this may not be applicable.	Yes □ Can't say □	No □ Does not apply □
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome.[ii]	Yes □ Can't say □	No □ □
1.10	The method of assessment of exposure is reliable.	Yes □ Can't say □	No □
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable.	Yes □ Can't say □	No □ Does not apply□
1.12	Exposure level or prognostic factor is assessed more than once	Yes □ Can't say □	No □ Does not apply □
CONFOUNDING			
1.13	The main potential confounders are identified and taken into account in the design and analysis.	Yes □ Can't say □	No □
STATISTICAL ANALYSIS			
1.14	Have confidence intervals been provided?	Yes □	No □
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	How well was the study done to minimise the risk of bias or confounding?	High quality (++) □ Acceptable (+) □ Unacceptable – reject 0	
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?	Yes ☐ Can't say ☐	No ☐
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?	Yes □	No □
2.4	**Notes.** Summarise the authors conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.		

Appendix 2: Quality scores for articles used in this review
SIGN Critical Appraisal Tool scores for Systematic Reviews

Quest	Reference (Author, year)	Verdugo et al. 2008	Kim and Park 2014	Gerritsen et al. 2002	Chen et al. 2015	Goodyear-Smith 2004	Marshall et al. 2007
1.1	The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper. Does this study do it?	Yes	No	Yes	Yes	Yes	Yes
1.2	A comprehensive literature search is carried out?	Yes	No	Yes	Yes	Yes	Yes
1.3	At least two people should have selected studies	Yes	Can't say	Yes	Yes	No	Yes
1.4	At least two people should have extracted the data	Yes	Can't say	Yes	Yes	No	Yes
1.5	The status of publication was not used as an inclusion criterion	Yes	Can't say	Can't say	No	No	Yes
1.6	The excluded studies are listed	Yes	No	No	No	No	Yes
1.7	The relevant characteristics of the included studies are provided	Yes	No	Yes	Yes	Yes	Yes
1.8	The scientific quality of the included studies was assessed and reported.	Yes	No	Yes	Yes	Yes	Yes
1.9	Was the scientific quality of the included studies used appropriately?	Yes	No	Yes	Yes	Yes	Yes
1.10	Appropriate methods are used to combine the individual study findings	Yes	No	Yes	Yes	Yes	Yes
1.11	The likelihood of publication bias was assessed appropriately	Yes	No	Yes	Yes	Yes	Yes
1.12	Conflicts of interest are declared	Yes	Yes	Yes	Yes	Yes	Yes
2.1	What is your overall assessment of the methodological quality of this review?	HQ(++)	R(0)	AQ(+)	AQ(+)	LQ(-)	HQ(++)
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes	Yes	Yes	Yes	Yes	Yes

SIGN Critical Appraisal Tool scores for controlled trials

Quest	Reference (Author, year)	Andreu et al. 2014	Atroshi et al. 2013	Awan et al. 2015	Bahrami et al. 2015	Bardak et al. 2009	Bilgici et al. 2010	Dammers et al. 2006	Dewi et al. 2009
1.1	The study addresses an appropriate and clearly focused question.	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
1.2	The assignment of subjects to treatment groups is randomised.	Can't say	Yes	Can't say	Yes	Can't say	Yes	Yes	Yes
1.3	An adequate concealment method is used.	No	Yes	No	Yes	Yes	Yes	Yes	Yes
1.4	The design keeps subjects and investigators 'blind' about treatment allocation.	Can't say	Yes	No	Yes	Yes	No	Yes	Yes
1.5	The treatment and control groups are similar at the start of the trial.	Yes	Yes	Yes	Can't say	Yes	Yes	Yes	Yes
1.6	The only difference between groups is the treatment under investigation.	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
1.9	All the subjects are analysed in the groups to which they were randomly allocated.	Can't say	Yes	Yes	Can't say	Yes	Yes	Yes	Can't say
1.10	Where the study is carried out at more than one site, results are comparable for all sites.	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
2.1	How well was the study done to minimise bias?	LQ(-)	HQ(++)	0	AQ(+)	HQ(++)	HQ(++)	AQ(+)	HQ(++)
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes	Yes	Can't say	Yes	Yes	Yes	Yes	Yes

Quest	Reference (Author, year)	Gurcay et al. 2009	Hui et al. 2004	Ismatullah 2013	Karadas et al. 2011	Karadas et al. 2012	Lee et al. 2014	Ly-Pen et al. 2005	Makhlouf et al. 2014
1.1	The study addresses an appropriate and clearly focused question.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
1.2	The assignment of subjects to treatment groups is randomised.	Yes	Can't say	Yes	Can't say	Can't say	Can't say	Yes	Yes
1.3	An adequate concealment method is used.	No	No	No	Yes	Yes	No	No	No
1.4	The design keeps subjects and investigators 'blind' about treatment allocation.	No	No	No	Yes	Yes	Can't say	No	No
1.5	The treatment and control groups are similar at the start of the trial.	Yes	Can't say	Yes	Yes	Yes	Can't say	Yes	Yes
1.6	The only difference between groups is the treatment under investigation.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
1.9	All the subjects are analysed in the groups to which they were randomly allocated.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
1.10	Where the study is carried out at more than one site, results are comparable for all sites.	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
2.1	How well was the study done to minimise bias?	AQ(+)	LQ(-)	AQ(+)	AQ(+)	AQ(+)	LQ(-)	AQ(+)	AQ(+)
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Quest	Reference (Author, year)	Peters-Veluthamaningal et al. 2010	Raeissadat & Soltani 2010	Seok & Kim 2013	Soltani et al. 2013	Ustun et al. 2013
1.1	The study addresses an appropriate and clearly focused question.	Yes	Yes	Yes	Yes	Yes
1.2	The assignment of subjects to treatment groups is randomised.	Yes	Can't say	Yes	Yes	Yes
1.3	An adequate concealment method is used.	Yes	No	No	No	No
1.4	The design keeps subjects and investigators 'blind' about treatment allocation.	Yes	No	No	Yes	No
1.5	The treatment and control groups are similar at the start of the trial.	Yes	Yes	Yes	Yes	Yes
1.6	The only difference between groups is the treatment under investigation.	Yes	Yes	Yes	Yes	Yes
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	Yes	Yes	Yes	Yes	Yes
1.9	All the subjects are analysed in the groups to which they were randomly allocated.	Yes	Yes	Yes	Yes	Yes
1.10	Where the study is carried out at more than one site, results are comparable for all sites.	Can't say	N/A	N/A	N/A	N/A
2.1	How well was the study done to minimise bias?	HQ(++)	LQ(-)	AQ(+)	HQ(++)	AQ(+)
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes	Yes	Yes	Yes	Yes

Appendix 3: Summary of systematic reviews included in this review

Author and year	SIGN Score	Studies (Patient No)	Outcome	Conclusions	Evidence				Grade
					1	2	3	4	
Chen et al. 2015	AQ (+)	10 RCTs	Clinical response, pain and function	• Local corticosteroid injections were more effective than placebo for clinical response. • Ulnar-I (ultrasound guided injection) is the most effective approach.	1	1	1	1	1++
Verdugo et al. 2008	HQ (++)	4 RCTs	Pain and function	• Surgical intervention is more effective than non-surgical interventions	0	1	0	1	1
				• Surgery in clearly superior to splinting	0	1	0	1	1
				• It is unclear whether local steroid injection is superior to surgery in the short term	0	1	0	1	1
Gerritsen	AC (+)	14 RCTs	Clinical improvement, symptoms	• Limited evidence that steroid injection is effective	0	1	1	1	1+
Goodyear-Smith 2004	LQ (-)	2 Systematic reviews 16 controlled trials 1 pre-post study	Pain and function	• Both injected and oral steroids have short-term benefits	0	0	1	1	1
Marshall et al. 2007	HQ (++)	10 RCTs	Pain and function	• Local steroid injection provides symptomatic relief at 1 month when compared to placebo	0	1	1	1	1+
				• The long term benefit of local steroid injection is unclear	0	1	1	1	1+
Kim and Park 2014	R(0)	30 studies (majority low quality)	Median nerve injury	• People with carpal tunnel syndrome may be at increased risk of injury during local steroid injection.	0	0	1	0	1-

Appendix 4: List of RCTS reported in the systematic reviews

RCTS	Systematic Reviews					
	Gerritsen et al. 2002	Goodyear-Smith 2004	Marshall et al. 2007	Verdugo et al. 2008	Chen et al. 2015	Kim and Park 2014
Ozdogan and Yazici 1984		x	x			
Lucantoni 1992			x			
Girlanda et al 1993	x					
Elbaz et al 1993		x				
Dammers et al 1993,		x				
Özdogan and Yazici 1988	x					
Dammers et al 1999,	x		x		x	x
O'Gradaigh and Merry 2000		x	x		x	
Wong et al 2001			x			
Celiker et al 2002,			x			
Sevim et al 2004,			x			
Armstrong et al 2004			x		x	
Wong et al 2005			x			
Gokoglu et al 2005,			x			
Aygül et al 2005			x			
Ly Pen et al 2005,				x		x
Hui et al 2005				x		
Habib et al 2006			x		x	
Peters-Veluthamaningal et al 2010,					x	
Karadas et al 2012,					x	
Andreu et al 2013,					x	
Atroshi et al 2013,						x
Ustün et al 2013,					x	x
Makhlouf et al 2014,					x	
Lee et al 2014,					x	

Appendix 5: Data extraction from RCTs used in this review

	Year	Study design	Injected steroid	Comparator/ control	Anaesthetic	Definition of Carpal Tunnel Syndrome	Outcome Measures	Results	Findings	Safety and Risk	Imaging	Patients
Andreu et al.	2014	RCT	Corticosteroid	Surgery	Not reported	Pain, tingling, burning, numbness, or some combination of these symptoms in the fingers in the distribution of the median nerve, that may radiate to the forearm, of at least 3 months' duration	Visual analogue scale for symptoms, nerve conduction studies	Although clinical outcome improved in a similar way in both groups, we found statistically significant improvement in 3 of 4 neurophysiologic parameters only in the surgery group, compared to baseline at 12 months' post treatment.	Although local corticosteroid and decompressive surgery are clinically effective in reducing symptoms of carpal tunnel syndrome, only surgery results	Not reported	None	163 wrists of 101 patients with a mean age of 50 years in the surgery group and 53 years in the injection group
Atroshi st al.	2013	RCT	Methylprednisolone	Saline +lidocaine	Lidocaine	Numbness or tingling in at least 2 of the 4 radial fingers according to the Katz diagnostic criteria	Δ carpal tunnel syndrome symptom severity score at 10 weeks, rate of surgery at 1 year, Δ carpal tunnel syndrome symptom severity score at 1 year, QuickDASH score, SF-6D score and treatment satisfaction at 10 weeks and 1 year	Improvement in CTS symptom severity scores at 10 weeks was greater in patients who received 80mg of methylprednisolone and 40mg of methylprednisolone than in those who received placebo (difference in change from baseline, -0.64 (95% CI, -1.06 to -0.21; P= 0.003) and -0.88 (CI, -1.30 to 0.46; P<0.001, respectively), but there were no significant differences at 1 year. The 1-year rates of surgery were 73%, 81%, and 92% in 80mg, 40mg methylprednisolone, and placebo groups respectively. Compared with patients who received placebo, those who received 80mg of methylprednisolone were less likely to have surgery (OR, 0.24; CI, 0.06 to 0.95)	Methylprednisolone injections for carpal tunnel syndrome have significant benefits in relieving symptoms at 10 weeks and reducing the rate of surgery 1 year after treatment, but 3 out of 4 patients had surgery within 1 year.	Not reported	None	A total of 111 (37 to each group) patients were randomly assigned to methylprednisolone (40mg or 80mg) and placebo groups.
Awan et al.	2015	RCT	Methylprednisolone	Surgery (Mini incision technique)	Not reported	Clinical diagnosis including both the Phalen test and Tinel's sign	Visual analogue scale (pain)	Local steroid injection was effective in 69% of cases while the mini incision technique was effective in 56.9% of cases (not a statistically significant difference)	The difference in pain after one month of the intervention was not statistically significant among patients receiving the steroid injection or surgery.	Not reported	None	A total of 116 patients mean age 32.8 ± 5.1 were randomly assigned to steroid injection or surgery
Bahrami et al.	2015	RCT	Corticosteroid	Progesterone	Lidocaine	Nocturnal numbness, paresthesia and electrodiagnostic tests	Visual analogue scale (pain), electrodiagnostic latency	Ten weeks after treatment, pain severity and median nerve sensory and motor latencies decreased while patients' functional status increased meaningfully in both groups. However, there were no meaningful differences between 2 groups. Pain severity was milder and duration of post-injection pain was shorter in the corticosteroid group.	Both treatments were effective in the short-term management of mild and moderate disease, clinically and elctrophysiologically. There were no significant differences in therapeutic effects between 2 groups.	Not reported	None	60 hands were carpal tunnel syndrome were included (32 corticiosteroid, 28 progesterone group)
Bardak wt al.	2009	RCT	Betamethasone	Tendon & nerve gliding exercises	Not reported	Patients were classified according to Lundborg classification as (1) early stage, characterised as nocturnal increase in the carpal tunnel tissue pressure; (2) intermediate stage, characterised as persistent symptoms, paresthesia, and numbness during the daytime; and (3) late stage, characterised as specialised, permanent impairment of sensorial and motor function.	Nerve conduction tests, phalen's test, Tinel's test	At the end of treatment, significant improvements in symptoms and functionality were detected in all groups. However, the recovery of patients in Groups 1 (steroid + splinting) and 2 (Group 1+ tendon & nerve gliding exercises) were found to be significantly greater than that of patients in group 3 (tendon & nerve gliding only).	In the intermediate stage of carpal tunnel syndrome, standard conservative treatment (corticosteroid injection and splinting) was an effective treatment to improve symptoms and functional status. Tendon and nerve gliding exercises alone were inferior to either standard conservative treatment alone or standard conservative treatment in combination with gliding exercises.	Not reported	None	A total of 111 patients mean age 49.1 ± 9.6 years (range 22-74 years).

	Year	Study design	Injected steroid	Comparator/ control	Anaesthetic	Definition of Carpal Tunnel Syndrome	Outcome Measures	Results	Findings	Safety and Risk	Imaging	Patients
Bilgici et al.	2010	RCT	Dexamethasone	Ultrasound	None	Carpal tunnel syndrome confirmed by standard electroodiagnosis	Nerve conduction tests, phalen's test, Tinel's test, two-point discrimination, grip strength, pain visual analogue scale, Boston Questionnaire, symptom severity scale	At the end of the study, a statistically improvement was obtained in all clinical parameters in the ultrasound group (VAS pain, severity of symptoms, functional status, grip strength ($p<0.001$ for each) and two point discrimination ($p<0.016$). Also the injection and splinting group showed significant improvements in all clinical parameters ($p<0.001$ for each), except for the grip strength. Additionally, significant improvements in the median nerve sensory conduction velocity and distal motor latency were also found in both groups at the end of the 8 week follow-up period. There was no significant difference between the groups except for grip strength.	Both ultrasound treatment and corticosteroid injection plus splinting were effective on the clinical symptoms and the electrophysiological findings of carpal tunnel syndrome. Ultrasound therapy may be an alternative treatment for carpal tunnel syndrome, particularly in patients who do not accept injection or splinting.	Adverse side effects were not recorded in either group, except for transient local injection pain in the injection group.	None	49 hands of 34 patients with carpal tunnel syndrome
Dammers et al.	2006	RCT	Methylprednisolone	20mg,40mg, 60mg methylpredn-isolone	None	Signs and symptoms of carpal tunnel syndrome >3 months confirmed by electrophysiological tests	One month after injection the randomised participants visited the outpatient department and were asked by another neurologist whether they had no symptoms or only minor symptoms that they considered so much improved that they felt treatment was no longer necessary. Further visits were planned for 3,6,9 and 12 months after the injection where the same question was asked.	There were no significant differences in the treatment response between the three randomised groups at one-year follow-up. In the 20, 40 and 60mg treatment groups, 56%, 53% and 73% of the patients respectively were free of important symptoms at 6 months follow-up. Of the patients treated with 1 or 2 injections 22% were finally referred to surgery within 1 year of the 1st treatment.	A single local injection of methylprednisolone 20, 40, 60 mg results in long lasting improvement in approximately ½ of the patients. There is a trend in favour of the highest dose. A 2nd injection may further reduce the number of patients requiring surgery	There were no side effects	None	132 patients were randomised into 3 groups; 20mg (n=45), 40mg (n=43) and 60mg (n=44) methylprednisolone
Dewi et al.	2009	RCT	Triamcinolone	Oral steroid	None	Rempel criteria: combination of clinical symptoms of pain or paresthesia or anesthesia in the distribution of median nerve or the presence of hand weakness, Tinel's or Phalen's test positive and the presence of abnormality in nerve conduction tests	Global symptom score, nerve conduction tests	The injection group showed significant improvement only at 2 weeks. Both groups improved in symptoms and neurophysiological parameters were significantly greater in the injection group.	In conclusion, this study shows that although oral administration of triamcinolone improved clinical symptoms and nerve conduction study parameters in carpal tunnel syndrome, local injection of triamcinolone had better efficacy in relieving symptoms and improving nerve conduction study parameters. However, in cases of patients refusing injection of triamcinolone, oral administration can be considered an alternative.	Not reported	None	50 patients mean age 53.6 years were randomised into oral or injection groups
Gurcay et al.	2009	RCT	Betamethasone	Meloxicam	None	Both clinical and electrodiagnostic findings	Functional status scale, Jebsen Taylor test, Nerve conduction	There was a significant improvement in functional status scale in both groups at the 3rd month. In the Jesbsen Taylor test, 'writing', 'picking up small common objects' and 'picking up large heavy objects' activities were improved in betamethasone injection group; 'writing' and 'stacking checkers' activities were improved in the NSAIDs group. Statistically significant improvement was observed in peak sensory conduction velocity and distal motor latency between the groups. Mixed nerve conduction velocity and compound sensory action potential were improved in the betamethasone group.	The results showed that neither if the groups demonstrated superior results. We conclude that local steroid injection and NSAIDs with concomitant use if wrist splints may offer patients with carpal tunnel syndrome variable and effective treatment options for the management of functional scores and nerve conduction parameters.	No complications or side effects to treatment were observed in any of the patients at the end of the treatment.	None	32 women ranging in age from 21 to 64 years (40.8 ± 11.2)

	Year	Study design	Injected steroid	Comparator/ control	Anaesthetic	Definition of Carpal Tunnel Syndrome	Outcome Measures	Results	Findings	Safety and Risk	Imaging	Patients
Hui et al.	2004	RCT	Methylprednisolone	Oral steroid	None	Electrophysio-logically confirmed	Global symptom score, surgery requirement	In the group treated with oral corticosteroids, 9 of 30 patients underwent surgery (30%) with 5 patients defaulting (16.7%), while in the injection group, 5 of 30 (16.7%) underwent surgery and 6 patients defaulted in the injection group.	In this study, we did not find any significant differences between the injection and the oral groups over the 80 -week (19 months) period of extended follow-up in terms of symptomatic relief. Those who underwent surgery showed a much better response, with a larger improvement in global symptom score as compared with those without surgery from the 15th month onwards. It is important to inform patients with carpal tunnel syndrome treated conservatively with steroid and splinting that, most cases, symptoms may recur in the long term	There were no long term adverse effects detected in either group	None	60 patients
Ismatullah	2013	RCT	Methylprednisolone	Surgery	None	Typical signs and symptoms including intermittent pain, parathesia & sensory deficit in median nerve distribution, usually worse at night as well as during daily activities , weakness of the abductor pollicis brevis muscle and atrophy of thenar muscles, positive phalen's test and positive tinel's sign, nerve conduction tests	Global symptom score (GSS)	The mean baseline GSS for the steroid group was 34.80 ± 8.15 and 35.45 ± for the surgery group. Two weeks after treatment, the mean GSS was 11.60 ± 6.90 for the steroid group and 12.50 ± 7.28. Four weeks after treatment, the mean GSS was 9.85 ± 6.39 for the steroid group and 7.30 ± 5.68. Twelve weeks after treatment, the mean GSS was 22.10 ± 6.90 for the steroid group and 5.45 ± 6.90. This trend shows that corticosteroid injection has a temporary effect on global symptom score in carpal tunnel syndrome whereas surgery had long-lasting effects.	Local corticosteroid injection provides temporary symptomatic relief whereas carpal tunnel release surgery results in lasting improvement of patients to the endpoint of 12-weeks period, in cases of carpal tunnel syndrome, shown in the short series of 40 patients with short-term follow-up.	There were no major complications in either of the two groups. A case of cellulitis was found with steroid injection group and a case of reflex sympathetic dystrophy was found in the surgery group.	None	40 participants aged between 24 and 66 years were randomly assigned to either local steroid injection or surgery
Karadas et al.	2011	RCT	Triamcinolone Acetonide	Procaine hydrochloride (Anaesthetic)	Procaine HCl	Symptoms of carpal tunnel, nocturnal paraesthesia, pain in median nerve distribution during activity, or numbness in the median nerve distribution, and positive electrophysiology study results	Nerve conduction test, pain VAS	Nerve conduction parameters and pain VAS scales improved significantly in each group 2 months after treatment (P< 0.05), and these improvements persisted at 6 months after treatment (P<0.05). Significant differences were not observed between group 1 (steroid) and group 2 (anaesthetic) or between groups 1 and 3 (steroid + anaesthetic) with respect to electrophysiologic findings at baseline or 2 or 6 months after treatment (P>0.05). Group 3 had better compound sensory action potential amplitude and sensory nerve conduction velocity scores than group 2 did at 6 months (P<0.05) and better pain VAS scores than group 2 at 2 and 6 months	Local Procaine HCl (anaesthetic) injection and steroid injection effectively reduced the symptoms of carpal tunnel syndrome and equally improved electrophysiologic findings. As such anaesthetic can be used in carpal tunnel syndrome patients in whom steroid use in contraindicated.	Not reported	None	99 patients (120 median nerves) mean age: group 1 48.02 ± 12.58, group 2 46.75 ±5.83, group 3 46.35 ± 12.38
Karadas et al.	2012	RCT	Triamcinolone Acetonide	Procaine hydrochloride (Anaesthetic) or Saline	Procaine HCl	Symptoms of carpal tunnel, nocturnal paraesthesia, pain in median nerve distribution during activity, or numbness in the median nerve distribution, and positive electrophysiology study results	Nerve conduction test, Boston carpal tunnel questionnaire, pain visual analogue scale	Clinical and electrophysiological evaluations improved significantly in groups 2 (steroid) and 3 (anaesthetic) at post treatment (p<0.05). No significant changes were observed in group 1 (saline) (P>0.05). Moreover, groups 2 and 3 had better scores than group 1 at 2 and 6 months post-treatment (P<0.05). There was no difference between groups 2 and 3 in terms of change scores of any of any terms at post-treatment (P>0.05)	In conclusion, steroid and procaine HCl injections are effective in carpal tunnel syndrome regarding short-and long-term outcomes compared with placebo injections, and local procaine HCl was as effective in reducing the symptoms of carpal tunnel syndrome and improving electrophysiological findings as steroid injection.	Not reported	None	57 patients (90 median nerves) mean age: group 1 48.40 ± 12.13, group 2 46.40 ±11.60, group 3 46.83 ± 5.97
Lee et al.	2014	RCT	Triamcinolone Acetonide	In-plane vs out-plane vs blind carpal tunnel injection	lidocaine	Mild to moderate carpal tunnel syndrome defined as slowing of the sensory conduction velocity and/or abnormal distal motor latency according to the validated electrophysiological severity scale	Nerve conduction test, sonographic findings, Boston Carpal Tunnel Questionnaire (BCTQ)	Subjective symptoms measured by BCTQ and median nerve conduction parameters showed significant improvement at 4 weeks in the in-plane ulnar approach group compared with the out-plane ulnar approach and blind injection. This improvement was still observed at 12 weeks. The flattening ratio and cross-sectional area of the median nerve showed a more significant decrease with the in-plane ulnar approach than with the out-plane ulnar approach and blind injection (P<0.05)	Although in-plane and out-plane ultra-sound guided carpal tunnel injection were more effective in improving electrodiagnistic, sonographic findings, and symptoms than blind injection, the in-plane ulnar approach was superior to the out-plane and blind injection in median-to-ulnar sensory nerve distal latency ratio SDL ratio, CSA, and BCTQ result. Ultra-sound guided local steroid injection using an in-plane ulnar approach in the carpal tunnel syndrome can be more effective than out-plane or blind injection	Vessel insult was not detected in ultrasound guided groups (out-plane ultrasound guided injection and in-plane ulnar approach) and nerve insult was not detected in in-plane ulnar approach	Ultrasound	44 patients (75 hands) were randomised into 3 groups

	Year	Study design	Injected steroid	Comparator/ control	Anaesthetic	Definition of Carpal Tunnel Syndrome	Outcome Measures	Results	Findings	Safety and Risk	Imaging	Patients
Ly-Pen et al.	2012	RCT	Paramethasone acetonide	Decompression surgery	None	Suggestive symptoms of carpal tunnel syndrome of at least 3 months duration.	Symptom VAS scale	In the intent-to-treat analysis, at 2-year follow-up, 60% of the wrists in the injection group vs 69% of the wrists in the injection group vs 69% in the surgery group reached a 20% response for nocturnal paraesthesias (P<0.001)	Both local steroid injection and surgical decompression are effective treatments in alleviating symptoms in primary carpal tunnel syndrome at 2-year follow up. Surgery has an additional benefit in the 2-year follow-up, although clinical relevance of those differences remains to be defined.	Not reported	None	A total of 163 wrists of 101 patients were included. Mean age: surgery- 50 ± 10; steroid- 53 ± 14
Makhlouf et al.	2014	RCT	Triamcinolone Acetonide	Anatomic landmark guidance (palpation)	Lidocaine	Hand numbness and tingling in the distribution of the median nerve, decreased grip strength, persistent hand pain, nocturnal hand pain	Pain VAS scale, time to next injection or referral for surgery, cost of procedure	Relative to conventional anatomic landmark palpation-guided methods, sonographic guidance for injection of the carpal tunnel resulted in 77.1% reduction in injection pain (p<0.01), a 63.3% reduction in pain scores at outcome (p<0.014), 93.5% increase in the responder rate (p<0.001), 84.6% reduction in the non-responder rate (p<0.001), a 71% increase in therapeutic duration (p<0.001), and a 59.3% ($150) reduction in cost/responder/year for a hospital outpatient (p<0.001)	The present study demonstrates that carpal tunnel injection performed with sonographic image guidance significantly and meaningfully reduces procedural pain, reduces pain scores at outcome, increases responder rates, and reduces non-responder rates while providing enhanced cost-effectiveness in certain practice venues and increased medical costs in others.	There were no complications	Sonography	77 carpal tunnel injections were undertaken in 64 participants; mean age palpation group: 52.2 ± 9.7; sonographic group 45.7 ± 14.8
Peters-Veluthamaningal	2010	RCT	Triamcinolone	NaCl injection	None	Symptoms and signs suggestive of carpal tunnel syndrome	Direct treatment response (0 =no response -3 =complete resolution), improvement perception (-2= much worse - +2= much better), symptom severity score, repeat injection or surgery referral, side effects	The injection group (n=36) had better outcomes than the placebo group (n=33) during short-term assessment for outcome measures treatment response, mean improvement of SSS-score and FSS-score and perceived improvement (p=0.01). The number of treat to achieve satisfactory partial treatment response or complete resolution of symptoms and signs was 3 (95% CI:1.83, 9.72). 49% of the injection group (17/35) had recurrences during follow-up.	Corticosteroid injections for carpal tunnel syndrome provided by general practitioners are effective regarding short-term outcomes when compared to placebo injections. The short term beneficial treatment effects of steroid injections deteriorated during the follow-up period of twelve months and half of the cohort of steroid-responders had recurrences.	There were no serious adverse events reported during short-term and long-term assessment. The most frequent reported side effects that had occurred within 1 week after blinded interventions and bailout treatment were steroid-flare: 14 events, hot flushes: 7 events, vaso-vagal symptoms: 3 events and menstrual irregularities: 2 events	None	69 participants were recruited by 20 general practitioners in 20 general practices. Mean age, placebo 57.60 ± 40.30, steroid 56.5 ± 15.14
Raeissadat & Soltani	2010	RCT	Hydrocortisone	Laser therapy	None	Nerve conduction tests	Pain visual analogue scale, orthodromic technique for assessment of the median nerve sensory nerve action potential (SNAP)	10 months after treatments, the mean pain severity was decreased 1.9cm in the injection group and 1.7cm in laser therapy group, the mean of median sensory peak latencies was decreased 0.4ms in the injection group and 0.25ms in the laser therapy group and the mean of motor onset latencies was decreased 0.15ms in both groups, with no significant difference between the observed treatments variables (P>0.05).	Low level laser therapy can be as effective as local injection in reducing pain and severity of disease (based on electrodiagnostic medicine classification) in patients with mild and moderate carpal tunnel syndrome even long term (after 10 months)	Not reported	None	65 hands were included, the mean age of participants was 43.9 years
Seok & Kim	2013	RCT	Triamcinolone	Extracorporeal shock wave therapy	Lidocaine	Nerve conduction tests	Nerve conduction tests, visual analogue scale, Levine self-assessment scale (VAS), Semmes-Weinstein test,	Both groups showed significant reduction in the VAS scale 1 to 3 months after treatment compared with baseline. Levine Self-assessment questionnaire the shockwave group showed significant reduction at 1 to 3 months after treatment, whereas the injection group showed showed a significant reduction at 3 months after treatment. For the nerve conduction parameters, there were mild but no significant improvements in the shockwave group, whereas the nerve conduction parameters were significantly improved in the injection group.	Extracorporeal shock wave therapy can be as useful as carpal tunnel syndrome injection for relieving symptoms of carpal tunnel syndrome. Furthermore, in contrast to corticosteroid injection, it has the merit of being non-invasive.	Not reported	Ultrasonography	36 eligible participants were randomised to receive either extracorporeal shock wave therapy or local corticosteroid injection.

	Year	Study design	Injected steroid	Comparator/ control	Anaesthetic	Definition of Carpal Tunnel Syndrome	Outcome Measures	Results	Findings	Safety and Risk	Imaging	Patients
Soltani et al.	2013	RCT	Hydrocortisone	Laser therapy	None	Clinical diagnosis	Severity of carpal tunnel (based on nerve conduction study parameters), pain visual analogue scale (VAS), symptoms of carpal tunnel syndrome (e.g. tingling or numbness)	Analyses showed favourable outcomes in both groups in terms of VAS and median distal motor and sensory latencies (P<0.001). Electrophysiologic studies did not imply any significant difference in the severity (Chi-squared test p=0.28), and change in the grade of the disease between the 2 groups. Also there was no significant difference the groups in mean VAS (Mann-Whitney test p=0.45), median motor distal latency (Mann-Whitney test p=0.70), 8 weeks after treatment.	Overall, we have good evidence that both corticosteroid and laser are advantageous in the short-term treatment of carpal tunnel syndrome. Both treatments provide satisfactory pain relief, restoring function, electrophysiological improvement, and are also well tolerated by patients. Steroid injection is partially invasive and painful and should be performed by an expert. However, with laser, frequent treatment sessions are not desirable.	Not reported	None	38 patients (50 hands) were enrolled in the study and randomised into one of 2 groups. Mean age was 47.4 ± 10
Üstun et al.	2013	RCT	Methylprednisolone	Ultrasound vs blind injection	None	Clinical diagnosis and neurophysiologic confirmation	Symptom severity and function, Boston carpal tunnel Questionnaire	The symptom severity and functional status scores improved significantly in both groups at 6 weeks after treatment, and these improvements persisted at 12 weeks after treatment (all P<0.05). The improvement in symptom severity scores in the ultra-sound guided group at 12 weeks was higher than in the palpation-guided group (P<0.05). Average time to symptom relief was shorter in the ultrasound guided group (P<0.05)	Although both ultrasound guided and blind steroid injections were effective in reducing the symptoms of carpal tunnel and improving the function, an earlier onset/better improvement of symptom relief suggests that ultra-sound guided steroid injection may be more effective than are blind injections in carpal tunnel syndrome.	The groups were similar in terms of side effects. Major side effects (nerve or blood vessel damage etc.) were not observed in both groups. Procedural pain was observed in 8 (34.7%) wrists in the blind injection group and 4 (17.3%) wrists in the ultra-sound guided group (P>0.05),	Ultrasound	46 patients, mean age 44 years were randomised to either ultrasound guided injection (n=23) or blind (landmark palpation) injection (n=23)