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Splinting for carpal tunnel syndrome (Review)

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Karjalainen TV, Lusa V, Page MJ, O'Connor D, Massy-Westropp N, Peters SE.
Splinting for carpal tunnel syndrome.
Cochrane Database of Systematic Reviews 2023, Issue 2. Art. No.: CD010003.
DOI: 10.1002/14651858.CD010003.pub2.

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[Intervention Review]

Splinting for carpal tunnel syndrome

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Editorial group: Cochrane Neuromuscular Group.
Publication status and date: New search for studies and content updated (conclusions changed), published in Issue 2, 2023.

Citation: Karjalainen TV, Lusa V, Page MJ, O'Connor D, Massy-Westropp N, Peters SE. Splinting for carpal tunnel syndrome. *Cochrane Database of Systematic Reviews* 2023, Issue 2. Art. No.: CD010003. DOI: 10.1002/14651858.CD010003.pub2.

ABSTRACT

Background

Carpal tunnel syndrome (CTS) is a compression neuropathy of the median nerve causing pain and numbness and tingling typically in the thumb, index and middle finger. It sometimes results in muscle wasting, diminished sensitivity and loss of dexterity. Splinting the wrist (with or without the hand) using an orthosis is usually offered to people with mild-to-moderate findings, but its effectiveness remains unclear.

Objectives

To assess the effects (benefits and harms) of splinting for people with CTS.

Search methods

On 12 December 2021, we searched the Cochrane Neuromuscular Specialised Register, CENTRAL, MEDLINE, Embase, AMED, CINAHL, ClinicalTrials.gov, and WHO ICTRP with no limitations. We checked the reference lists of included studies and relevant systematic reviews for studies.

Selection criteria

Randomised trials were included if the effect of splinting could be isolated from other treatment modalities. The comparisons included splinting versus no active treatment (or placebo), splinting versus another disease-modifying non-surgical treatment, and comparisons of different splint-wearing regimens. We excluded studies comparing splinting with surgery or one splint design with another. We excluded participants if they had previously undergone surgical release.

Data collection and analysis

Review authors independently selected trials for inclusion, extracted data, assessed study risk of bias and the certainty in the body of evidence for primary outcomes using the GRADE approach, according to standard Cochrane methodology.

Main results

We included 29 trials randomising 1937 adults with CTS. The trials ranged from 21 to 234 participants, with mean ages between 42 and 60 years. The mean duration of CTS symptoms was seven weeks to five years. Eight studies with 523 hands compared splinting with no active intervention (no treatment, sham-kinesiology tape or sham-laser); 20 studies compared splinting (or splinting delivered along with

another non-surgical intervention) with another non-surgical intervention; and three studies compared different splinting regimens (e.g. night-time only versus full time).

Trials were generally at high risk of bias for one or more domains, including lack of blinding (all included studies) and lack of information about randomisation or allocation concealment in 23 studies.

For the primary comparison, splinting compared to no active treatment, splinting may provide little or no benefits in symptoms in the short term (< 3 months). The mean Boston Carpal Tunnel Questionnaire (BCTQ) Symptom Severity Scale (SSS) (scale 1 to 5, higher is worse; minimal clinically important difference (MCID) 1 point) was 0.37 points better with splint (95% confidence interval (CI) 0.82 better to 0.08 worse; 6 studies, 306 participants; low-certainty evidence) compared with no active treatment. Removing studies with high or unclear risk of bias due to lack of randomisation or allocation concealment supported our conclusion of no important effect (mean difference (MD) 0.01 points worse with splint; 95% CI 0.20 better to 0.22 worse; 3 studies, 124 participants). In the long term (> 3 months), we are uncertain about the effect of splinting on symptoms (mean BCTQ SSS 0.64 better with splinting; 95% CI 1.2 better to 0.08 better; 2 studies, 144 participants; very low-certainty evidence).

Splinting probably does not improve hand function in the short term and may not improve hand function in the long term. In the short term, the mean BCTQ Functional Status Scale (FSS) (1 to 5, higher is worse; MCID 0.7 points) was 0.24 points better (95% CI 0.44 better to 0.03 better; 6 studies, 306 participants; moderate-certainty evidence) with splinting compared with no active treatment. In the long term, the mean BCTQ FSS was 0.25 points better (95% CI 0.68 better to 0.18 worse; 1 study, 34 participants; low-certainty evidence) with splinting compared with no active treatment.

Night-time splinting may result in a higher rate of overall improvement in the short term (risk ratio (RR) 3.86, 95% CI 2.29 to 6.51; 1 study, 80 participants; number needed to treat for an additional beneficial outcome (NNTB) 2, 95% CI 2 to 2; low-certainty evidence).

We are uncertain if splinting decreases referral to surgery, RR 0.47 (95% CI 0.14 to 1.58; 3 studies, 243 participants; very low-certainty evidence).

None of the trials reported health-related quality of life.

Low-certainty evidence from one study suggests that splinting may have a higher rate of adverse events, which were transient, but the 95% CIs included no effect. Seven of 40 participants (18%) reported adverse effects in the splinting group and 0 of 40 participants (0%) in the no active treatment group (RR 15.0, 95% CI 0.89 to 254.13; 1 study, 80 participants).

There was low- to moderate-certainty evidence for the other comparisons: splinting may not provide additional benefits in symptoms or hand function when given together with corticosteroid injection (moderate-certainty evidence) or with rehabilitation (low-certainty evidence); nor when compared with corticosteroid (injection or oral; low certainty), exercises (low certainty), kinesiology taping (low certainty), rigid taping (low certainty), platelet-rich plasma (moderate certainty), or extracorporeal shock wave treatment (moderate certainty). Splinting for 12 weeks may not be better than six weeks, but six months of splinting may be better than six weeks of splinting in improving symptoms and function (low-certainty evidence).

Authors' conclusions

There is insufficient evidence to conclude whether splinting benefits people with CTS. Limited evidence does not exclude small improvements in CTS symptoms and hand function, but they may not be clinically important, and the clinical relevance of small differences with splinting is unclear. Low-certainty evidence suggests that people may have a greater chance of experiencing overall improvement with night-time splints than no treatment. As splinting is a relatively inexpensive intervention with no plausible long-term harms, small effects could justify its use, particularly when patients are not interested in having surgery or injections.

It is unclear if a splint is optimally worn full time or at night-time only and whether long-term use is better than short-term use, but low-certainty evidence suggests that the benefits may manifest in the long term.

PLAIN LANGUAGE SUMMARY

Splinting for carpal tunnel syndrome

Review question

This Cochrane review aimed to compare the benefits and harms of wrist splints with no treatment or other types of treatment for people with carpal tunnel syndrome (CTS).

Background

CTS is a condition where one of the two main nerves in the wrist is compressed. This can lead to pain in the hand and wrist as well as numbness and tingling in the thumb, index and middle finger. Severe compression may result in wasting of hand muscles and loss of dexterity of the hand. CTS is more common in women and in people over 50 years of age.

Many people undergo surgery to treat CTS, though usually non-surgical treatments, such as splinting, corticosteroid injections (a drug that reduces inflammation) or exercises are offered first. Splinting involves immobilisation of the wrist in a neutral (straight) position, usually leaving the fingers and thumb free to move.

Study characteristics

We collected and analysed all relevant studies to answer our review question and found 29 studies that assessed the safety and benefit of splinting for people with CTS. The average ages of participants were between 42 and 60 years, the number of participants was 1937, and 81% were women. Most had mild-to-moderate symptoms.

Key results

When worn for fewer than three months, splinting may not improve CTS symptoms and probably does not improve hand function compared with no intervention. However, people who used a night-time splint tended to report that overall they felt improvement compared with those that did not use a splint.

In the longer term (more than 3 months), we are still uncertain of the benefits of splinting due to few studies and inconsistent findings across similar studies. We cannot say for certain if splinting provides meaningful improvements in symptoms or function.

We are also uncertain if splinting reduces the need for surgery because only three studies reported this outcome. Splinting may cause temporary side effects such as difficulty in falling asleep or transient tingling after removal of the splint; none of the trials reported any serious side effects. None of the studies reported whether splints improved quality of life.

Some studies assessed if splinting improves outcomes when delivered alongside other treatments. The results suggested that splinting may make little or no difference to outcomes when given together with corticosteroid injection or with various types of rehabilitation.

Splinting was compared with other types of treatments. Splinting does not appear to improve outcomes compared with corticosteroid (injection or oral), exercises, kinesiology taping (stretchy tape), rigid taping, and probably does not improve outcomes compared with platelet-rich plasma (concentrate of plasma and platelet derived from blood) or extracorporeal shock wave treatment (pulses of high energy sound).

Some studies compared different splint-wearing regimens. One study found that six months of splinting may improve symptoms and function compared with six weeks of splinting. Another study found that full-time splinting may not improve outcomes compared to night-time splinting.

Author's conclusions

Currently, there is limited evidence supporting the use of wrist splints to treat CTS as there are few studies and their findings are inconsistent. While it appears that splinting may not make symptoms worse or result in side effects, splinting may provide little or no benefit for CTS symptoms and hand function, especially in the short term (less than 3 months). One study suggests that night-time splinting may increase the chance of overall improvement compared with no treatment. Benefits of splinting may occur after months of use, but we need well-designed research studies to establish how effective splinting is, and to identify the best way to use splints (night-time or full-time use; long-term or short-term use).

Splinting is relatively inexpensive and has no known long-term side effects. Therefore, even small benefits may justify its use in people who are not interested in invasive interventions such as surgery.

Certainty of evidence

People in the studies were aware of their treatment. This knowledge can produce more favourable assessments of benefit than when people are unaware of treatment ('blinded'). In the few studies that examined the same treatments and outcomes, findings were inconsistent.

The evidence is up-to-date to December 2021.

SUMMARY OF FINDINGS

Summary of findings 1. SPLINT compared to NO ACTIVE TREATMENT for carpal tunnel syndrome

SPLINT compared to NO ACTIVE TREATMENT for carpal tunnel syndrome

Patient or population: carpal tunnel syndrome
Setting: outpatient clinics in Italy, Thailand and Turkey; hospital clinic in Australia; education and research hospital in Turkey; auto assembly plant in the USA
Intervention: SPLINT
Comparison: NO ACTIVE TREATMENT

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with NO ACTIVE TREATMENT	Risk with SPLINT				
CTS symptoms (Boston CTS questionnaire) - short-term improvement: < 3 months Scale: 1 to 5, higher is worse	The mean CTS symptoms-severity was **2.37 points**	MD **0.37 points better** (0.82 better to 0.08 worse)	-	306 (6 RCTs)	⊕⊕⊖⊖ **Low**[a,b]	Splint may not improve CTS symptoms in the short term. Absolute difference 9.25% better (20.5% better to 2% worse) with splint[c]
CTS symptoms (Boston CTS questionnaire) - long-term improvement: > 3 months Scale: 1 to 5, higher is worse	The mean CTS symptoms severity was **2.48 points**	MD **0.64 points better** (1.2 better to 0.08 better)	-	144 (2 RCTs)	⊕⊖⊖⊖ **Very low**[a,b,d]	We are uncertain if splint improves CTS symptoms in the long term. Absolute difference 16% better (30% better to 2% better) with splint
Function (Boston CTS questionnaire) - long-term improvement: > 3 months Scale: 1 to 5, higher is worse	The mean function was **1.77 points**	MD **0.25 points better** (0.68 better to 0.18 worse)	-	34 (1 RCT)	⊕⊕⊖⊖ **Low**[a,d]	Splint may not improve hand function in the long term. Absolute difference 6.25% better (17% better to 4.5% worse) with splint
Overall improvement (improved/not improved or worsened) - short-term improvement: < 3 months	Study population		RR 3.86 (2.29 to 6.51)	80 (1 RCT)	⊕⊕⊖⊖ **Low**[a,d]	More people may report overall improvement in the short term with a splint than without a splint. Absolute risk difference 75% better (61% better to 89% better) with splint. NNTB 2 (95% CI 2 to 2)
	250 per 1000	**965 per 1000** (573 to 1000)				

Health-related quality of life - long-term improvement: > 3 months	No studies reported this outcome.		-	(0 RCTs)	-	Not estimable. We are uncertain about the effect.
Adverse effects	Study population		RR 15.00 (0.89 to 254.13)	80 (1 RCT)	⊕⊕⊖⊖ **Low**[a,d]	Splint may increase risk of transient adverse effects. Absolute risk difference 17% worse (5% worse to 30% worse) with splint
	Not calculable from the study data. 0/40 (0%)	Not calculable from the study data. 7/40 (18%)				
Referral for surgery	Study population		RR 0.47 (0.14 to 1.58)	243 (3 RCTs)	⊕⊖⊖⊖ **Very low**[a,e]	We are uncertain if splint can reduce referral for surgery. Absolute risk difference 4% better (11% better to 3% worse) with splint
	79 per 1000	**37 per 1000** (11 to 125)				

*__The risk in the intervention group__ (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD**: mean difference; **RCT**: randomised controlled trial; **RR:** risk ratio; **CTS**: carpal tunnel syndrome

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]Downgraded one level for high risk of bias in the included studies (lack of blinding)
[b]Downgraded one level for inconsistency (the estimates were not consistent between the studies)
[c]Absolute risk difference calculated as risk in control group - risk in the splinting group
[d]Downgraded for imprecision (the 95% did not exclude clinically relevant effects)
[e]Downgraded twice for very serious imprecision (95% CIs included substantial effect in both directions)

BACKGROUND

Description of the condition

Carpal tunnel syndrome (CTS) refers to a condition where the median nerve function is compromised because of compression in the carpal tunnel. Symptoms of CTS include pain in the wrist and hand which can spread to the arm and paraesthesiae (numbness or tingling) in the thumb, index, middle and radial half of the ring finger (Atroshi 1999). Advanced CTS can result in loss of sensitivity in the thumb, index and middle finger, thenar muscle weakness and atrophy and subsequent loss of dexterity (Keir 2005). Suspected risk factors for CTS include diabetes, obesity, menopause, arthritis, hypothyroidism, smoking, and pregnancy (Padua 2016).

The course of CTS is not predictable: some people progress from intermittent paraesthesia to more constant paraesthesia, and eventual thenar atrophy, others experience intermittent exacerbation of sensory symptoms over many years, while others experience spontaneous (and lasting) remission (Braun 1989). There is no reliable data on the number of people who experience spontaneous remission, as such information is often based on assessment using nerve conduction studies, which have been found to correlate weakly with clinical outcomes (Hardoim 2009; Padua 1999; Resende 2003).

The reported prevalence and incidence of CTS has varied across studies depending on the diagnostic criteria used. Results of a Swedish study suggest that the prevalence of CTS in the general population is 3.8% for clinically diagnosed cases and 2.7% for electrophysiologically confirmed cases (Atroshi 1999), and as high as 7.8% in the U.S. working population (Dale 2013). Incidence was 1.7/1000 person years in Finland, and it is associated with age and sex (Pourmemari 2018). People aged less than 25 years accounted for 2.4% of people presenting to Australian general practices with the condition between 2000 and 2009, compared to people aged 45 to 64 years who accounted for 45.5% of these cases (Charles 2009). CTS is reported to affect more women than men (Padua 2016): 67% of CTS encounters at Australian general practices were in women (Charles 2009), and women in their fourth and fifth decades were four times more likely to suffer from CTS compared to men (Atroshi 1999). CTS has been reported to occur more frequently in some professions, where there is frequent grasping, forceful grasping and flexed wrist postures, or exposure to vibration from hand-held tools (Palmar 2007).

Description of the intervention

Treatment options for CTS are either surgical or non-surgical. Carpal tunnel release (CTR) has been reported as the most common surgery in the United States, with more than 400,000 CTRs performed annually, with an estimated total cost to the healthcare system of $2 billion (Concannon 2000; Huisstede 2010). Surgical treatment is usually offered to those with advanced CTS, who have constant symptoms, severe sensory disturbance, or thenar motor weakness. Non-surgical treatments are recommended as an initial treatment for those who have symptoms without evidence of denervation, cannot undergo surgery, or have intermittent symptoms of mild-to-moderate CTS. Non-surgical treatment for CTS includes various interventions such as wrist splinting (with or without the hand included), taping the wrist (e.g. kinesiology taping), injections (including corticosteroid or platelet-rich plasma (PRP)) into the carpal canal, exercises, yoga, therapeutic ultrasound, laser, acupuncture, activity or ergonomic modification, oral medication, and vitamins (Dong 2020; Geler Kulcu 2016; Muller 2004; O'Connor 2012; Ostergaard 2020).

Splinting generally immobilises the wrist joint by using an external orthosis. The splint usually leaves the fingers and thumb free to move, but some designs may include the fingers. The wrist is generally positioned in a neutral position in the splint; although, the precise angle has yet to be determined, between less than 20 degrees extension and closer to zero degrees has been found to be optimal (Burke 1994). This splint may be worn either at night-time only or during both the night and day. A thermoplastic splint may be custom fitted to the person with CTS by an occupational therapist, physiotherapist, or hand therapist. Sometimes, a softer, adjustable splint may be fitted; these splints can either be custom-made or purchased off the shelf. Some splints may permit a restricted range of motion (Wang 2017).

How the intervention might work

In people with CTS, the wrist is usually splinted in a neutral position (i.e. with a straight wrist). When the wrist is in a neutral position, the pressure on the median nerve as it passes through the carpal tunnel is at its lowest. When the wrist is flexed or extended, the pressure increases (Gelberman 1984). As many people sleep with wrists in a flexed position, splinting at night maintains the wrist in the optimal position to reduce pressure within the carpal tunnel. Some have considered whether splinting the hand, in addition to the wrist, provides an additional benefit, as flexion of the fingers may further increase pressure in the carpal tunnel, through movement of the lumbricals, a group of small finger muscles, into the carpal tunnel (Manente 2001).

Why it is important to do this review

CTS creates significant impairment in terms of pain and functional use of the hand. Work days missed due to CTS result in financial loss to both the individual and society. Workers with a CTS diagnosis missed a median of 28 days of work to recuperate (U.S. Bureau of Labor Statistics 2016). For individuals suffering from symptomatic CTS, the direct and indirect costs can average USD 40,000 per year for life (Gabrielli 2020).

Following the publication of the previous versions of this review (O'Connor 2003; Page 2012b), which could not draw firm conclusions on the effect of splinting, the evidence base for all non-surgical interventions for CTS has grown. Splinting is a common first-line intervention for those with less severe symptoms or for those who do not wish to pursue more invasive treatment options, yet its efficacy is still unclear (Page 2012b). Cochrane systematic reviews of local corticosteroid injections (Marshall 2007), surgical versus non-surgical treatment (Verdugo 2008), different surgical treatment options (Scholten 2007), therapeutic ultrasound (Page 2013), ergonomic interventions (O'Connor 2012), acupuncture (Choi 2018), low-level laser therapy (Rankin 2017), exercise and mobilisation interventions (Page 2012a) for CTS already exist, and up-to-date Cochrane systematic reviews of other non-surgical interventions for CTS (e.g. splinting, oral drugs) are required. Given the personal and financial impact of CTS, there is a need to ascertain the efficacy of splinting for the treatment of CTS.

OBJECTIVES

To assess the effects (benefits and harms) of splinting for people with carpal tunnel syndrome.

METHODS

Criteria for considering studies for this review

Types of studies

All published and unpublished randomised controlled trials (RCTs) and quasi-RCTs were eligible for inclusion regardless of publication status and whether they contained outcomes of interest or not. We did not use any language or publication date restrictions or limit the setting of the trials.

Types of participants

All study participants had a diagnosis of carpal tunnel syndrome (CTS), as defined by the authors of each study. We excluded studies that included participants who had previous surgery for CTS.

Types of interventions

We included all splinting interventions, including static (immobilisation), dynamic (allowing a limited range of motion within the splint), or splints aimed at stretching the transverse carpal ligament.

Comparators included no treatment, placebo and other non-surgical interventions. We also included studies comparing different splinting regimens (i.e. different time periods, or night versus day versus full time).

We excluded the following.

- Studies comparing splinting with other non-surgical treatments that did not have plausible biological mechanism of action to modify the disease or interventions that could be considered as symptom-modifying interventions. These included, for example, acupuncture, electroacupuncture, yoga, or topical flax seed oil, interferential current, transcutaneous electrical nerve stimulation and phonophoresis;
- Studies in which the effect of splinting could not be isolated from the other treatment modalities. That is, splinting was delivered alongside another active treatment and the control group did not receive the same active co-intervention;
- Studies comparing splinting with surgical treatment (as these are reviewed elsewhere, Verdugo 2008);
- Studies comparing various splint designs since these comparisons do not inform stakeholders if splints can provide benefits in people with CTS. Moreover, these comparison yield treatment estimates between a specific type of splints and these estimates are likely not applicable. However, these comparisons may be included in future updates if splinting is found to be efficacious.

Types of outcome measures

The outcomes reported in this review have been modified from the original review (O'Connor 2003) and its most recent update (Page 2012b); see Differences between protocol and review. For this update, we used CTS symptoms (continuous outcome) as the primary outcome, since global improvement is infrequently used and the Boston Carpal Tunnel Questionnaire (BCTQ) is a validated responsive measure used in most studies (Leite 2006; Multanen 2020). We prioritised the BCTQ Symptoms Severity Scale for symptoms and used pain (Visual Analogue Scale (VAS) or Numeric Rating Scale (NRS)) as a secondary source of data if the BCTQ was not measured or reported (5 of 11, or 45% items in the BCTQ Symptom Severity Scale are measuring pain).

Furthermore, we did not consider the electrodiagnostic outcomes (e.g. sensory or motor nerve conduction velocity) in this update, as their clinical relevance is unclear (Schrijver 2005; see Differences between protocol and review).

We planned to prioritise one-year follow-up for long-term outcomes, but since no studies reported multiple long-term time points, we did not have to choose between various time points.

Primary outcomes

- CTS symptoms (prioritising BCTQ Symptom Severity Scale) at:
  - Short term (up to 3 months prioritising the time closest to 3 months); and
  - Long term (over 3 months).

Secondary outcomes

1. Function (CTS-specific or hand-specific patient-reported outcome measure) at:
   a. Short term (up to 3 months, prioritising the time closest to 3 months); and
   b. Long term (over 3 months).
2. Overall improvement of symptoms (dichotomised from global scale (e.g. Likert) or binary outcome categorising participants as improved) at:
   a. Short term (up to 3 months, prioritising the time closest to 3 months); and
   b. Long term (over 3 months).
3. Health-related quality of life at:
   a. Short term (up to 3 months, prioritising the time closest to 3 months); and
   b. Long term (over 3 months).
4. Adverse effects at the final time point of the study.
5. Referral for surgery (number of participants who were referred to surgery or operated, at the final time point of the study).

Search methods for identification of studies

Electronic searches

On 11 December 2020 and 12 December 2021, the Cochrane Neuromuscular Information Specialist searched the following databases for this version of the review:

- the Cochrane Neuromuscular Specialised Register via the Cochrane Register of Studies (CRS-Web) (until Search Date; Appendix 1)
- the Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Register of Studies (CRS-Web) (until Search Date; Appendix 2)
- MEDLINE (1946 to 10 December 2021; Appendix 3)
- Embase (1974 to Week 49 2021; Appendix 4)
- AMED (1985 to December 2021; Appendix 5)

- CINAHL Plus (1937 to 12 December 2021; Appendix 6)
- ClinicalTrials.Gov (until Search Date; Appendix 7)
- WHO ICTRP (until Search Date; Appendix 8)

There was no limitation to date of publication, language, publication status or document type.

Searching other resources

We browsed the reference lists of all included trials and relevant reviews for further relevant studies.

Data collection and analysis

The review authors followed the recommended strategies for data collection and analysis as documented in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2021).

Selection of studies

Review authors (TK, VL, SP) working in pairs independently selected trials for possible inclusion based on the review inclusion criteria (study is an RCT or quasi-RCT; study investigates splinting versus other non-surgical treatment, no treatment, or placebo, or different splinting regimens for CTS). We then retrieved trials that were potentially eligible for full-text evaluation to determine whether they met the inclusion criteria. The authors resolved any disagreement via discussion. We also searched PubMed for relevant errata or retraction statements for the included studies, and collated several references related to the same study.

Data extraction and management

Review authors (TK, VL, SP, MP, NMW, DOC) working in pairs independently extracted data from each study using a standardised data extraction form. Authors resolved any discrepancies by discussion. We pilot-tested the data extraction form and modified it accordingly before use. We recorded the following details.

- Participant details (number of participants randomised and analysed, sex, age, duration of symptoms).
- Inclusion and exclusion criteria, as well as CTS diagnostic criteria.
- Types of interventions used and details of the comparator.
- Outcomes, including the type and timing of measures used.
- Source of funding and investigators' conflicts of interest.

One review author (VL) compiled all data and entered the data into RevMan Web.

Assessment of risk of bias in included studies

Review authors (TK, VL, SP, MP, NMW, DOC) working in pairs independently assessed the risk of bias of the included studies using The Cochrane Collaboration's risk of bias tool, as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We assessed the following domains for risk of bias based on information extracted from the reports of the included studies.

- Random sequence generation.
- Allocation concealment.
- Blinding of participants and personnel.
- Blinding of outcome assessment.
- Incomplete outcome data (defined separately for data measured at 3 months or less, and after 3 months).
- Selective reporting.
- Other sources of bias. (e.g. inappropriate unit of analysis).

The review authors rated each domain as being at 'low risk of bias', 'unclear risk of bias' or 'high risk of bias'. We resolved any discrepancies through discussion.

Measures of treatment effect

We used Cochrane Review Manager (RevMan) software to perform data analyses (Review Manager 2020). We expressed results as the risk ratio (RR) and 95% confidence interval (CI) for dichotomous outcomes and mean difference (MD) with 95% CI for continuous outcomes when the same measurement tool was used to measure the same outcome across all studies in the meta-analysis.

When studies used different measurement instruments for the same outcome domain, we used a standardised mean difference (SMD) as a summary measure. We then back-transformed the SMD to the typical outcome measure (multiplying the SMD and its 95% CI by a typical among-person standard deviation (SD) (e.g. the SD of the control group at baseline from the most representative trial)). When the outcome measures had a different direction in a meta-analysis (e.g. higher versus lower is better), we reversed the values so that the direction was the same in all studies.

For dichotomous outcomes, we calculated the number needed to treat for an additional beneficial outcome (NNTB) or number needed to treat for an additional harmful outcome (NNTH) as 1/risk difference when the analysis showed benefit or harm for splinting. NNTB are reported in whole numbers, rounded up.

We set statistical significance at $P < 0.05$ for all outcomes.

Unit of analysis issues

We sought information about the unit of randomisation used (i.e. wrists or participants, where participants with bilateral CTS received the same intervention for both wrists). In studies that randomised wrists, we sought information about whether each participant's wrist was allocated to different treatments, or whether there was no constraint that each participant's wrist be allocated to different treatments. We preferred participant-level data whenever it was available. If the authors had randomised wrists and did not report results at the participant level and had not adjusted the analyses for clustering, we considered this a possible source of bias in the 'other bias' domain.

In case of multi-arm studies, we compared the splinting arm with other eligible arms in separate analyses, avoiding double-counting the same participants in the total number of the analysed participants.

Dealing with missing data

The review authors sought relevant missing information about the study design or results from the study investigators, where possible. We noted in the Characteristics of included studies tables when authors were contacted for additional data. When SDs of the mean were not reported, we calculated them based on the standard error of the mean, 95% CIs of the mean, reported P values, interquartile range, or range. When

the SD was calculated using other measures, we noted this in the Characteristics of included studies table in the notes section.

Assessment of heterogeneity

We assessed clinical diversity by determining whether the characteristics of participants, interventions, outcome measures and timing of outcome measurement were similar across studies. Statistical heterogeneity was assessed by visual inspection of the forest plots and using the Chi^2 statistic and the I^2 test (Higgins 2002). We interpreted the I^2 statistic using the following as an approximate guide (Deeks 2021).

- 0% to 40% might not be important heterogeneity.
- 30% to 60% may represent moderate heterogeneity.
- 50% to 90% may represent substantial heterogeneity.
- 75% to 100% may represent considerable heterogeneity.

Assessment of reporting biases

To assess publication bias, we intended to generate funnel plots if the review included at least 10 studies examining the same treatment comparison (Page 2021). To assess outcome reporting bias, we searched protocols of trials on the clinical trials register (clinicaltrials.gov), and at the International Clinical Trials Registry Platform of the World Health Organization (apps.who.int/trialssearch), to compare with the corresponding published RCTs (Dwan 2008; Dwan 2011). When the study was not registered, or we could not identify a published protocol, we deemed the study to be at unclear risk of selective reporting bias.

Data synthesis

We defined the following review questions based on the protocol in the previous version and based on the identified comparisons as follows.

- Splint versus no active intervention
- Splint versus corticosteroid injection
- Splint versus oral steroid
- Splint plus corticosteroid injection versus corticosteroid injection
- Splint versus exercise
- Stretching splint versus stretching exercises
- Splint versus kinesiology taping
- Splint versus rigid tape
- Splint versus platelet-rich plasma (PRP)
- Splint versus extracorporeal shockwave therapy (ESWT)
- Dynamic splint plus rehabilitation versus rehabilitation
- Splint for six weeks versus splint for 12 weeks
- Splint for six weeks versus splint for six months
- Night-time splinting versus full-time splinting

We pooled the results of studies with similar characteristics (participants, interventions, outcome measures and timing of outcome measurement) in a random-effects meta-analysis (inverse variance method, DerSimonian-Laird between-study variance estimator, Wald-type method for calculating the 95% CI of the summary effect) for each comparison to provide effect estimates for each outcome that was measured and reported. The primary analysis included all eligible studies. Where we could not pool data, we presented the results as reported by the authors narratively.

We used minimal clinically important difference (MCID) values to assess the clinical importance of differences in patient-reported outcomes. A wide range of values have been reported as the MCID for the BCTQ Symptom Severity Scale (0.16 to 1.45) and Functional Status Scale (0.47 to 1.6) (De Kleermaeker 2018). We considered a one-point difference as MCID for the BCTQ Symptom Severity Scale and 0.7 points for the Functional Status Scale (Kim 2013). Furthermore, we used 0.074 points difference as MCID for the EQ-5D (Walters 2005).

Subgroup analysis and investigation of heterogeneity

We performed no subgroup analyses in this update, as data were not available, but we planned to do subgroup analyses regarding the primary outcome according to the severity of CTS symptoms and sex as per the previous review protocol.

- Severity of CTS symptoms: early (E), intermediate (I) and advanced (A) symptoms (Szabo 1992)
- Sex: male and female

Sensitivity analysis

To assess the robustness of our findings, we planned sensitivity analyses for studies with low risk of bias in all domains versus those with high or unclear; and low risk of selection bias versus high or unclear risk for the primary comparison (splint versus no active treatment). Since all studies were at high risk of detection and performance bias, we only conducted the latter sensitivity analysis regarding the primary outcome (CTS symptoms).

Summary of findings and assessment of the certainty of the evidence

We presented all outcomes for the primary comparison (splint compared to no active treatment) in the Summary of findings 1 and in the additional table (Table 1). We included one effect estimate for each of our primary and secondary outcomes (see Types of outcome measures) and included an overall grading of the evidence related to each of the main outcomes, using the GRADE approach (Schünemann 2017). For binary outcomes, we presented the assumed control group risk and relative risk in the splinting group. We also calculated and noted the absolute risk difference between the intervention and control group, as calculated in GRADEpro GDT (GRADEpro GDT 2021), expressed as a percentage. For continuous outcomes, we reported the weighted mean value for the control group (i.e. mean1 * sample size1 + mean2 * sample size2 + meanx * sample sizex/sum of sample sizes). The absolute difference is expressed as the mean difference (MD) with 95% confidence intervals. We also calculated the relative difference (relative to the scale of the measurement instrument; i.e. MD divided by the scale of the measure and expressed as a percentage).

Two review authors (TK, VL) assessed the certainty of the evidence as 'high', 'moderate', 'low', or 'very low' using the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the body of evidence. We used GRADEpro software to prepare the Summary of findings table (GRADEpro GDT 2021). We reported decisions to downgrade the certainty of evidence in the footnotes of the Summary of findings table and in the 'Results' section for each

outcome. For comparisons and outcomes that were not included in the Summary of Findings table, the certainty of evidence was reported in the results section.

RESULTS

Description of studies

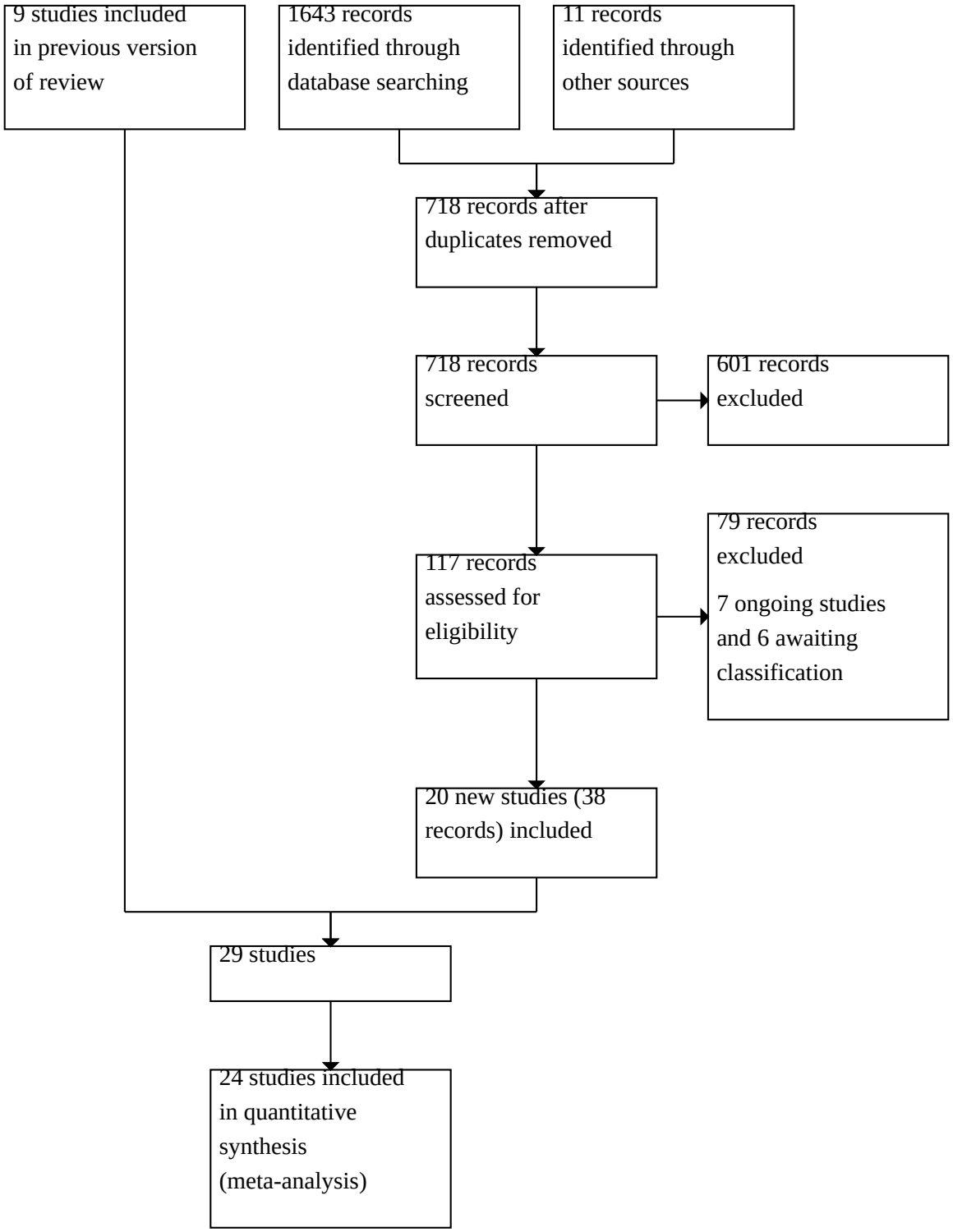
See Characteristics of included studies; Characteristics of excluded studies.

Results of the search

Eight of the 19 trials included in the previous Cochrane Review met the inclusion criteria for this updated review due to the restriction in scope from the original review (De Entrambasaguas 2006, Madjdinasab 2008; Manente 2001; Mishra 2006; Premoselli 2006; Sevim 2004; Walker 2000; Werner 2005). One study awaiting classification in the previous Cochrane Review is now included in the updated review (Taspinar 2007).

The search was updated on 12 December 2021, and we identified 1643 new records, assessed 81 potentially eligible full texts and finally included 20 new studies (Akturk 2018; Chesterton 2018; De Moraes 2021; Eraslan 2014; Gatheridge 2020; Geler Kulcu 2016; Hall 2013; Jaladat 2017; Kocaoglu 2017; Oncu 2014; Rioja Toro 2012; Sanaee 2017; Schmid 2012; So 2018; Ulucakoy 2020; Wang 2017; Willis 2016; Wu 2017; Yazdanpanah 2012) (Figure 1).

Figure 1. 1 - reasons for exclusion: in 5 studies the effect of splinting cannot be isolated from that of the other intervention delivered alongside it; in 29 studies splint applied to each study group; 7 studies compare treatment methods which we defined as not relevant for this review; 5 studies were not a randomised trial



Six studies are currently awaiting assessment for the following reasons:

1. It is unclear if the study is a randomised controlled trial (RCT) (Bhuva 2019; Riasi 2015);
2. Results are not yet published in a format that allows for risk of bias assessment and data extraction (Baklaci 2015; Soon 2015);
3. Two clinical trials from the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal were marked as completed (IRCT2014020416485N1; ISRCTN22916517), but we found no published articles.

We identified seven ongoing studies that seemed to meet our inclusion criteria (Atroshi 2019; and six clinical trials from World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal and ClinicalTrials.gov: IRCT20120716010297N5; IRCT20200219046552N1; JPRN-UMIN000017952; NCT04017390; NCT04515966; NCT04993703).

A flow diagram of the study selection process is presented in Figure 1.

Included studies

Twenty-nine RCTs, published between and 2000 and 2021, were included in this review.

Participants

The 29 included studies comprised 1937 randomised participants. Some participants had bilateral carpal tunnel syndrome (CTS) and, thus, the studies included 2362 wrists. Three-hundred-and-thirty (19%) participants were men, 1372 (81%) were women, and 235 randomised participants (from 9 studies) did not report the sex distribution (De Entrambasaguas 2006; Gatheridge 2020; Geler Kulcu 2016; Hall 2013; Manente 2001; Sanaee 2017; Schmid 2012; Sevim 2004; Werner 2005).

The trials size varied from 21 to 234 participants. Participants' mean age ranged between 42 and 60 years; one study (Yazdanpanah 2012) did not report the age of participants. The mean duration of CTS symptoms varied from seven weeks to five years in 16 studies; 13 studies did not report the mean duration of symptoms (Chesterton 2018; De Moraes 2021; Eraslan 2014; Jaladat 2017; Madjdinasab 2008; Manente 2001; Oncu 2014; Premoselli 2006; Rioja Toro 2012; Walker 2000; Werner 2005; Willis 2016; Yazdanpanah 2012). Most trialists excluded people with diabetes or rheumatoid arthritis, except for seven studies that included participants with these health conditions (Chesterton 2018; Hall 2013; Taspinar 2007; Ulucakoy 2020; Walker 2000; Werner 2005; Wu 2017). Most of the studies reported having pregnancy as exclusion criteria (Boonhong 2017; Chesterton 2018; Gatheridge 2020; Geler Kulcu 2016; Hall 2013; Jaladat 2017; Madjdinasab 2008; Manente 2001; Mishra 2006; Oncu 2014; Sanaee 2017; Schmid 2012; Sevim 2004; So 2018; Taspinar 2007; Ulucakoy 2020; Wang 2017; Werner 2005; Willis 2016; Wu 2017). One study specifically focused on pregnant women as their population of interest (Yazdanpanah 2012).

Participants in the included studies started with moderate impairment measured by the Boston Carpal Tunnel Questionnaire (BCTQ) Symptom Severity Scale (1 to 5, higher is worse) or Functional Status Scale (1 to 5, higher is worse). The mean symptom severity score at baseline was 2.79 (range from 1.66 to 3.65, data available n = 1689, 23 studies), and the mean functional status score was 2.37 (range from 1.25 to 4.05, data available n = 1577, 22 studies).

Interventions

Splint wear regimen and duration

Treatments varied in duration, type of splint and splint-wearing regimen. The duration of splint use ranged from one week of nocturnal use (Schmid 2012), to one year of nocturnal use (Sevim 2004), with about half of studies (15 of 29) prescribing a regimen of between two and six weeks. The most common regimen was nocturnal wear (23 of 29 studies, in 8 of which also daytime wear was recommended whenever possible). One study specifically compared night-time use with full-time use (Walker 2000). One study did not report how the splint was worn (Kocaoglu 2017), and in two studies the duration of splint use was unclear (Rioja Toro 2012; Wu 2017).

Fifteen studies reported that they monitored compliance/adherence with splint use (Boonhong 2017; Chesterton 2018; Gatheridge 2020; Hall 2013; Manente 2001; Mishra 2006; Premoselli 2006; Sanaee 2017; Schmid 2012; Sevim 2004; So 2018; Walker 2000; Wang 2017; Werner 2005; Willis 2016). The reported compliance/adherence to splint use mainly varied from full to partial (we presented specific information for each study in the Notes section of Characteristics of included studies). Some studies excluded participants who did not comply with splint use from follow-up (Premoselli 2006; Sanaee 2017). One study formed the control group from the subset of participants who did not comply with the splint regimen (Sevim 2004), but we combined data from the splinting group and this control group to perform an intention-to-treat analysis.

Types of splints

Splints were both custom-made and commercially available. All splints involved wrist support at angles of 'neutral' to 20° of wrist extension. Most splints did not describe joint involvement other than the wrist, except for the MANU hand brace developed by Manente 2001 (fingers 2 to 5 were splinted), and in some cases the MCP joints were also splinted in a 'neutral' position. In one study, instead of immobilising the wrist, the 'Dynasplint' applied pressure across the base of the hand in order to stretch the transverse carpal ligament (Willis 2016). One study used a "limited dynamic wrist splint" that allowed the wrist to move between 15° of flexion and extension without radial or ulnar deviation of the wrist (Jaladat 2017).

Co-interventions

Ten studies measured the effect of splints delivered with some other non-surgical intervention: education (Hall 2013), ergonomic education (Boonhong 2017; Werner 2005), an exercise programme (Akturk 2018), a physical therapy programme (consisting of heat application-ultrasound-transcutaneous electrical nerve stimulation (TENS) and strengthening exercises) (Eraslan 2014), usual rehabilitation including activity or ergonomic modifications, nerve and tendon gliding exercises, massage, carpal bones and nerve mobilisations, stretches of the upper extremity and flexor retinaculum (Jaladat 2017), tendon and nerve gliding exercises (Geler Kulcu 2016; Oncu 2014), corticosteroid injection (Wang 2017),

NSAID, B_1 and B_6, paraffin bath, ultrasound underwater and grip exercise (Sanaee 2017).

Outcomes

Primary outcome: CTS symptoms

We extracted symptom severity scores of the BCTQ (scale 1 to 5, higher is worse; Levine 1993), whenever possible. In one study (Sevim 2004), symptoms were measured by the Neurological Symptom Score (scale 0 to 3, higher is worse). Symptom severity was measured in 25 studies (Akturk 2018; Boonhong 2017; Chesterton 2018; De Moraes 2021; Eraslan 2014; Gatheridge 2020; Geler Kulcu 2016; Hall 2013; Jaladat 2017; Kocaoglu 2017; Manente 2001; Mishra 2006; Oncu 2014; Premoselli 2006; Rioja Toro 2012; Sanaee 2017; Schmid 2012; Sevim 2004; So 2018; Taspinar 2007; Ulucakoy 2020; Walker 2000; Wang 2017; Werner 2005; Willis 2016; Wu 2017). However, two of the studies did not report the scores and did not respond to queries (Willis 2016; Rioja Toro 2012).

Secondary outcomes

Secondary outcomes were function; overall improvement; health-related quality of life score (HRQoL); adverse effects; and referral for surgery.

Function

The most commonly assessed secondary outcome was the BCTQ functional status score (scale 1 to 5, higher is worse), measured in 23 studies (Akturk 2018; Boonhong 2017; Chesterton 2018; De Moraes 2021; Eraslan 2014; Gatheridge 2020; Geler Kulcu 2016; Hall 2013; Jaladat 2017; Kocaoglu 2017; Manente 2001; Mishra 2006; Oncu 2014; Premoselli 2006; Rioja Toro 2012; Sanaee 2017; Schmid 2012; So 2018; Taspinar 2007; Ulucakoy 2020; Walker 2000; Wang 2017; Wu 2017).

Overall improvement

Overall improvement, using any measure where participants indicate the overall/global intensity of their complaints compared with baseline, was reported in three studies (De Moraes 2021; Manente 2001; Wang 2017). So 2018 reported satisfaction score on a five-point scale.

HRQoL

Two studies reported HRQoL (Chesterton 2018 by EQ-5D-5L and Taspinar 2007 by Health Assessment Questionnaire).

Adverse events

Adverse effects of splint and other non-surgical interventions for CTS were measured and reported in nine studies (Boonhong 2017; Chesterton 2018; De Entrambasaguas 2006; De Moraes 2021; Manente 2001; Mishra 2006; Sevim 2004; Taspinar 2007; Wu 2017).

Referral for surgery

Referral for surgery was measured in nine studies (Chesterton 2018; De Moraes 2021; Gatheridge 2020; Hall 2013; Manente 2001; Premoselli 2006; Sanaee 2017; Werner 2005; Willis 2016). However, this was incompletely reported in Hall 2013.

Twenty-eight studies measured outcomes at short-term follow-up (up to 3 months after treatment). Eight studies measured outcomes at long-term follow-up (more than 3 months after treatment) (Chesterton 2018; De Moraes 2021; Premoselli 2006; Sanaee 2017; Sevim 2004; Werner 2005; Willis 2016; Wu 2017).

Unit of analysis

The unit of analysis was the wrist in 11 studies (Akturk 2018; De Entrambasaguas 2006; Gatheridge 2020; Geler Kulcu 2016; Mishra 2006; Oncu 2014; Rioja Toro 2012; Sanaee 2017; Taspinar 2007; Walker 2000; Yazdanpanah 2012), and some or all participants in these studies had bilateral CTS.

1. In seven of these studies (Gatheridge 2020; Geler Kulcu 2016; Mishra 2006; Oncu 2014; Sanaee 2017; Walker 2000; Yazdanpanah 2012), randomisation occurred at the level of participants, and the same intervention was delivered to both wrists.
2. In Rioja Toro 2012, the authors performed double randomisation at the wrist level (firstly to laser/placebo laser groups and then the same participants to splint/no splint groups), and each participant's wrists could be allocated to the same or different treatments.
3. It was unclear in three studies whether participants were randomised at the level of the person or the wrist or if people with bilateral CTS received the same or different interventions for each wrist (Akturk 2018; De Entrambasaguas 2006; Taspinar 2007).

The unit of analysis was the participant in 18 studies (Boonhong 2017; Chesterton 2018; De Moraes 2021; Eraslan 2014; Hall 2013; Jaladat 2017; Kocaoglu 2017; Madjdinasab 2008; Manente 2001; Premoselli 2006; Schmid 2012; Sevim 2004; So 2018; Ulucakoy 2020; Wang 2017; Werner 2005; Willis 2016; Wu 2017), even if some or all participants in these studies had bilateral CTS.

1. In 11 of these studies, only one side was assessed at follow-up for people with bilateral CTS (Boonhong 2017; Chesterton 2018; De Moraes 2021; Hall 2013; Manente 2001; Premoselli 2006; Schmid 2012; Sevim 2004; So 2018; Wang 2017; Werner 2005). Chesterton 2018 also permitted treatment of the non-study hand using the research clinical protocol.
2. In three studies, some included participants had bilateral CTS; however, no clear information was provided with respect to how the trial investigators dealt with and accounted for bilateral CTS in their study design and analysis (outcomes were analysed at the participant level) (Eraslan 2014; Madjdinasab 2008; Ulucakoy 2020).
3. It was unclear in three studies whether any participant had bilateral CTS and how the study dealt with bilateral CTS if such was present (outcomes were analysed at the participant level) (Jaladat 2017; Kocaoglu 2017; Willis 2016).
4. Wu 2017 included only people with unilateral CTS in the study and analysis.

Funding

Eight studies reported receiving financial support through various sources (Boonhong 2017; Chesterton 2018; Manente 2001; Schmid 2012; Walker 2000; Werner 2005; Willis 2016; Wu 2017). Three studies declared that no financial support was received (De Moraes 2021; Oncu 2014; Ulucakoy 2020). Eighteen studies did not report information related to the funding (Akturk 2018; De Entrambasaguas 2006; Eraslan 2014; Gatheridge 2020; Geler Kulcu 2016; Hall 2013; Jaladat 2017; Kocaoglu 2017; Madjdinasab 2008;

Mishra 2006; Premoselli 2006; Rioja Toro 2012; Sanaee 2017; Sevim 2004; So 2018; Taspinar 2007; Wang 2017; Yazdanpanah 2012).

Excluded studies

In total, we excluded 72 studies after review of the full publication. Reasons for exclusion of studies are given in the 'Characteristics of excluded studies' table. The most common reasons for exclusion were:

1. Both groups followed a similar splinting regimen, thus the effect of splinting could not be assessed.
2. The effect of splinting could not be isolated from that of the other concomitant treatment(s) delivered alongside (i.e. splint was delivered with another treatment that was not applied in the control group).
3. The study compared treatment methods not relevant for this review (see Types of studies): splint and nerve- and tendon-gliding exercises versus gabapentin and nerve- and tendon-gliding exercises; splint versus surgery; splint versus yoga; splint versus acupuncture; splint versus interferential current; splint versus transcutaneous electrical nerve stimulation; splint versus ultrasound and transcutaneous electrical stimulation; splint versus flax seed oil topical gel; splint versus phonophoresis; splint versus phonophoresis with corticosteroid; splint versus phonophoresis with NSAID.

Risk of bias in included studies

For details of risk of bias in the included studies, see the 'Characteristics of included studies' tables and Figure 2.

Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

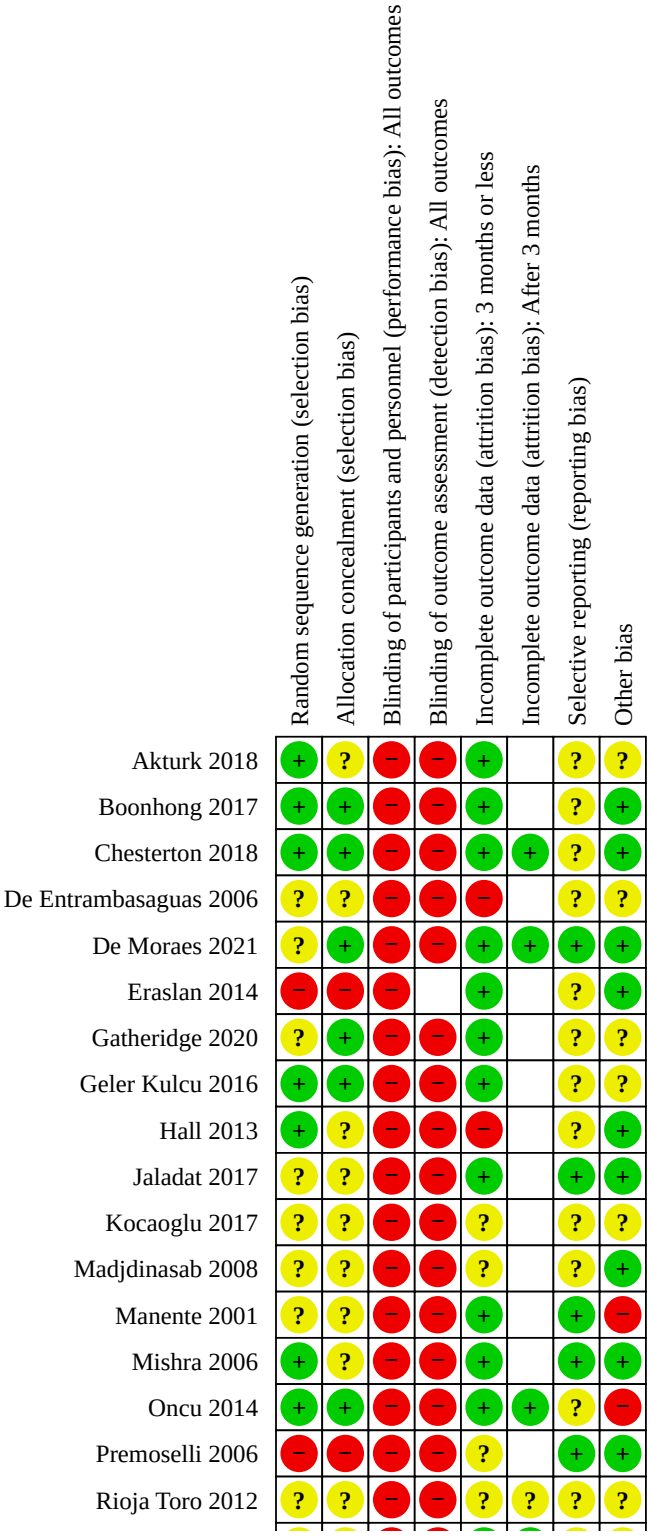
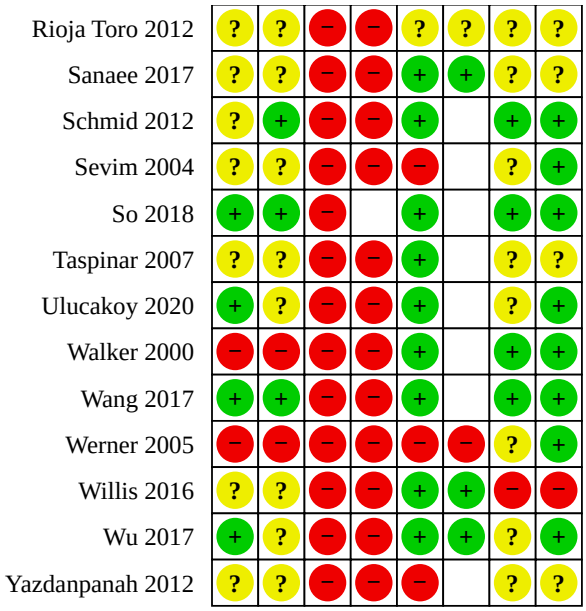


Figure 2. (Continued)



Allocation

Eleven studies reported a method of random sequence generation that we deemed adequate, and we rated them as at low risk of bias (Akturk 2018; Boonhong 2017; Chesterton 2018; Geler Kulcu 2016; Hall 2013; Mishra 2006; Oncu 2014; So 2018; Ulucakoy 2020; Wang 2017; Wu 2017). In four studies (Eraslan 2014; Premoselli 2006; Walker 2000; Werner 2005), the method of sequence generation was a type of alternation (i.e. non-random), so we rated these studies at high risk of bias. Fourteen studies did not report enough information regarding the method of random sequence generation, therefore, we rated the risk of bias for this domain as unclear (De Entrambasaguas 2006; De Moraes 2021; Gatheridge 2020; Jaladat 2017; Kocaoglu 2017; Madjdinasab 2008; Manente 2001; Rioja Toro 2012; Sanaee 2017; Schmid 2012; Sevim 2004; Taspinar 2007; Willis 2016; Yazdanpanah 2012).

Nine studies described an adequate type of allocation concealment (Boonhong 2017; Chesterton 2018; De Moraes 2021; Gatheridge 2020; Geler Kulcu 2016; Oncu 2014; Schmid 2012; So 2018; Wang 2017). In four studies (Eraslan 2014; Premoselli 2006; Walker 2000; Werner 2005), the method of allocation was a type of alternation (i.e. non-random), and therefore allocation was not concealed (high risk). Sixteen studies did not report enough information regarding the method of allocation concealment. Therefore, we rated the risk of bias for this domain as unclear (Akturk 2018; De Entrambasaguas 2006; Hall 2013; Jaladat 2017; Kocaoglu 2017; Madjdinasab 2008; Manente 2001; Mishra 2006; Rioja Toro 2012; Sanaee 2017; Sevim 2004; Taspinar 2007; Ulucakoy 2020; Willis 2016; Wu 2017; Yazdanpanah 2012).

Blinding

All participants were aware of the allocation. Although 12 studies reported blinding of assessors or clinicians (Akturk 2018; Boonhong 2017; De Entrambasaguas 2006; Geler Kulcu 2016; Oncu 2014; Premoselli 2006; Sanaee 2017; Schmid 2012; Sevim 2004; Wang 2017; Werner 2005; Wu 2017), we rated blinding of participants (performance bias) at high risk of bias in all 29 studies because all outcomes considered for this review were either self-reported or could be influenced by the participant knowing the allocation. Participants must have known which group they belonged to from the differences between splinting and control interventions, and no study reported using a placebo splint.

Incomplete outcome data

We rated outcome data collected at three months or less at low risk of bias in 20 studies (Akturk 2018; Boonhong 2017; Chesterton 2018; De Moraes 2021; Eraslan 2014; Gatheridge 2020; Geler Kulcu 2016; Jaladat 2017; Manente 2001; Mishra 2006; Oncu 2014; Sanaee 2017; Schmid 2012; So 2018; Taspinar 2007; Ulucakoy 2020; Walker 2000; Wang 2017; Willis 2016; Wu 2017). In these 20 studies there was either a) no missing data or b) the amount of and reasons for missing data were similar across groups.

In four studies, we rated attrition bias as unclear because the trial authors reported insufficient information on dropouts or reasons for missing data (Kocaoglu 2017; Madjdinasab 2008; Premoselli 2006; Rioja Toro 2012). In five studies, we rated attrition bias as high because of either a) high or imbalanced loss to follow-up (De Entrambasaguas 2006; Hall 2013; Werner 2005; Yazdanpanah 2012) or b) change of study protocol (in Sevim 2004 a control group was formed from the participants who did not adhere to the study protocol).

We rated six studies reporting outcome data at the long term at low risk of bias (Chesterton 2018; De Moraes 2021; Oncu 2014; Sanaee 2017; Willis 2016; Wu 2017) because there were either a) no missing data or b) the amount and reasons for missing data were similar across groups. We rated one trial as being at unclear risk because the reporting of information on dropouts or reasons for missing data was insufficient (Rioja Toro 2012). We rated one study as being

at high risk of bias because of large attrition, which varied between reported outcomes (Werner 2005).

Selective reporting

In 19 studies, we rated the risk of bias from selective reporting as unclear, because, while all the outcomes specified in the 'Methods' section of the trial publication were reported, no study had a published protocol or trial registry entry, or studies did not report some outcomes as predefined (it was unclear in these instances if such reporting was because of the nature of findings) (Akturk 2018; Boonhong 2017; Chesterton 2018; De Entrambasaguas 2006; Eraslan 2014; Gatheridge 2020; Geler Kulcu 2016; Hall 2013; Kocaoglu 2017; Madjdinasab 2008; Oncu 2014; Rioja Toro 2012; Sanaee 2017; Sevim 2004; Taspinar 2007; Ulucakoy 2020; Werner 2005; Wu 2017; Yazdanpanah 2012). In nine studies, we rated the risk of selective reporting as being at low risk of bias, because all the outcomes specified were reported and the study protocol or registry record was available (De Moraes 2021; Jaladat 2017; Manente 2001; Mishra 2006; Premoselli 2006; Schmid 2012; So 2018; Walker 2000; Wang 2017). In one study, we rated the risk of selective reporting as being at high risk of bias, due to partial reporting of prespecified outcomes (Willis 2016).

Other potential sources of bias

We judged three studies as being at high risk of other potential sources of bias because of either a potential conflict of interest or unit of analysis issues (Manente 2001; Oncu 2014; Willis 2016).

Effects of interventions

See: **Summary of findings 1** SPLINT compared to NO ACTIVE TREATMENT for carpal tunnel syndrome

1. Splint versus no active treatment

Eight studies compared splinting with no active treatment (Boonhong 2017; Geler Kulcu 2016; Hall 2013; Manente 2001; Oncu 2014; Premoselli 2006; Rioja Toro 2012; Werner 2005). Four of the studies instructed the participants to wear the splints only at night-time (Manente 2001; Premoselli 2006; Oncu 2014; Werner 2005), while three studies prescribed full-time splinting (Boonhong 2017; Geler Kulcu 2016; Hall 2013). One study did not report sufficient information to be included in the meta-analysis (Rioja Toro 2012).

Primary outcome: CTS symptoms

For short-term follow-up, we found low-certainty evidence (downgraded once for risk of bias and once for inconsistency) from six studies indicating that splinting may not improve CTS symptoms compared with no active treatment (measured with the BCTQ Symptom Severity Scale from 1 to 5 points, higher is worse, minimal clinically important difference (MCID) value = 1 point). The heterogeneity may be explained by the risk of selection bias; studies at high risk found an effect, while studies at low risk did not. The mean symptom severity score was 2.37 with no active treatment and 0.37 points better with splint (95% confidence interval (CI) 0.82 better to 0.08 worse; 6 studies, 306 participants, I^2 = 93%; Analysis 1.1; Summary of findings 1). Geler Kulcu 2016 and Manente 2001 reported data at four weeks; Hall 2013 reported data at eight weeks; Boonhong 2017 and Premoselli 2006 reported data at three months; and Oncu 2014 reported data at 25 days, two months and three months, from which we used the three-month data.

For long-term follow-up, we downgraded the certainty of evidence to very low (once for risk of bias, once for inconsistency, and once for imprecision as the 95% CI overlapped with the MCID value). Thus, we are uncertain about the effect of splinting after three months. The mean symptom severity score was 2.48 with no active treatment and 0.64 points better with the splint (95% CI 1.2 better to 0.08 better, 2 studies, 144 participants, I^2 = 83%; Analysis 1.1; Summary of findings 1). Premoselli 2006 reported data at six months, but Werner 2005 at 12 months.

Sensitivity analysis

After removal of studies with an unclear or high risk of selection bias, the effect moved towards splinting having a null effect. At short-term follow-up, the mean difference (MD) in the BCTQ symptom severity score between splint and no active treatment group was 0.01 points worse (95% CI 0.20 better to 0.22 worse, 3 studies, 124 participants, I^2 = 1%). At long-term follow-up, there were no studies with a low risk of selection bias.

We could not study the effect of blinding in a sensitivity analysis because we did not identify any studies that had blinded the participants.

Secondary outcomes

1) Function

For short-term follow-up, we found moderate-certainty evidence (downgraded once for risk of bias) from six trials that splinting probably does not provide a clinically meaningful improvement in hand function (measured by the BCTQ Functional Status Scale from 1 to 5 points, higher is worse, MCID value = 0.7 points) compared with no active treatment. The mean functional status score was 1.97 with no active treatment and 0.24 points better with splint (95% CI 0.44 better to 0.03 better, 6 studies, 306 participants, I^2 = 66%; Analysis 1.2; Summary of findings 1). Geler Kulcu 2016 and Manente 2001 recorded data at four weeks; Hall 2013 recorded data at eight weeks; Boonhong 2017, Premoselli 2006 and Oncu 2014 recorded data at three months.

At long-term follow-up, we graded the certainty of evidence as low (downgraded once for risk of bias and once for imprecision as only 1 study with a low number of participants, n = 34, contributed to the analysis and the 95% CIs touched the MCID value). The mean functional status score was 1.77 with no active treatment and 0.25 points better with the splint (95% CI 0.68 better to 0.18 worse, 1 study, 34 participants; Analysis 1.2; Summary of findings 1).

2) Overall improvement

One study reported overall improvement (measured by the Global Impression Change Questionnaire, rated in four categories from 'moderate' or 'much' improvement to 'worsening') at short-term follow-up (Manente 2001). Since the other studies did not measure this outcome, we could not assess the inconsistency. Manente 2001 also measured the BCTQ scores and was one of the studies reporting the benefit of splinting in the BCTQ Symptom Severity Scale analysis that had high heterogeneity (Analysis 1.1).

We rated the evidence for overall improvement as low certainty (downgraded once for risk of bias and once for imprecision,

because only one study with 80 participants contributed to the analysis). The evidence indicates that night-time splinting may result in higher rates of overall improvement compared with no active treatment. In the splinting group, 40 of 40 participants (100%) improved versus 10 of 40 participants (25%) in the no active treatment group, corresponding to a risk ratio (RR) of 3.86 (95% CI 2.29 to 6.51, 1 study, 80 participants) (Analysis 1.3; Summary of findings 1). This equates to a number needed to treat for an additional beneficial outcome (NNTB) of 2 (95% CI 2 to 2).

This outcome was not reported at long-term follow-up.

3) Health-related quality of life

None of the studies in this comparison reported this outcome.

4) Adverse effects

Two studies reported this outcome (Boonhong 2017; Manente 2001). Participants who were prescribed a splint reported higher rate of adverse effects (difficulty in falling asleep, n = 3, and transient paraesthesias after removal of the splint, n = 4); however, the 95% CI overlap suggested that there could be no difference between groups. The certainty of evidence was downgraded to low (once for risk of bias and once for imprecision due to low number of events and overlapping 95% CIs suggesting there could be no effect).

Boonhong 2017 reported no serious adverse effects in either group and that "some minor adverse outcomes of splint treatment including itching and feelings of discomfort were reported" but did not report the exact numbers. Thus, this trial did not contribute to analyses.

In Manente 2001, adverse effects were reported by seven of 40 participants (17.5%) in the splinting group and by 0 of 40 participants (0%) in the no active treatment group corresponding to an RR of 15.0 (95% CI 0.89 to 254.13, 1 study, 80 participants) (Analysis 1.4; Summary of findings 1).

5) Referral for surgery

Three studies reported this outcome (Manente 2001; Premoselli 2006; Werner 2005). We downgraded the certainty of evidence to very low (once for risk of bias, and twice for very serious imprecision, as 95% CIs include substantial effect in both directions). In the splinting group, 4 of 129 participants (3%) were referred to surgery compared to 9 of 114 participants (8%) in the no active treatment group, corresponding to an RR of 0.47 (95% CI 0.14 to 1.58, 3 studies, 243 participants, I^2 = 0%) (Analysis 1.5; Summary of findings 1). Hall 2013 reported that 19 of 30 participants (63%) had decided not to pursue surgical intervention after the CTS conservative treatment programme (which implies that 11 of 30 (37%) participants had opted for surgery). However, the outcome was not reported for the control group.

2. Splint versus corticosteroid injection

Eight studies were included in this comparison (Chesterton 2018; De Entrambasaguas 2006; De Moraes 2021; Kocaoglu 2017; Sevim 2004; So 2018; Taspinar 2007; Yazdanpanah 2012), of which one study did not report sufficient data to be included in the meta-analysis (Yazdanpanah 2012).

Primary outcome: CTS symptoms

Moderate-certainty evidence (downgraded once for risk of bias) indicated that corticosteroids may provide a small but clinically unimportant benefit compared with splinting at short-term follow-up. Although the MD favoured corticosteroid injection, the 95% CIs excluded clinically meaningful benefit for injection. The mean symptom severity score (measured by the BCTQ, scale from 1 to 5, higher is worse, MCID value = 1 point) was 1.88 with corticosteroids and 0.28 points worse (95% CI 0.04 worse to 0.51 worse; 5 studies, 459 participants, I^2 = 63%) with splints (Analysis 2.1 shows standardised mean difference (SMD) due to various measures at long term).

At long-term follow-up, the certainty of evidence was downgraded to low (due to the risk of bias and unexplained inconsistency), indicating that there may not be clinically important benefit between splint and corticosteroid injection. The SMD was 0.09 (95% CI -0.66 to 0.83, 3 studies, 437 participants, I^2 = 93%) (Analysis 2.1). This translates to 0.06 points worse (95% CI 0.42 better to 0.52 worse) symptom severity score in the BCTQ Symptom Severity Scale with splinting compared with corticosteroid injection (using standard deviation (SD) of 0.63 at baseline from Chesterton 2018).

Secondary outcomes

1) Function

Moderate-certainty evidence (downgraded once for risk of bias) indicates that splinting probably provides little or no benefits compared with corticosteroid injection at short-term follow-up. The mean functional status score measured by the BCTQ Functional Status Scale (scale from 1 to 5, higher is worse, MCID value = 0.7 points) was 1.76 for those who received a corticosteroid injection, and 0.16 points worse (95% CI 0.04 better to 0.36 worse, 5 studies, 459 participants, I^2 = 44%) for those who were prescribed a splint (Analysis 2.2).

At long-term follow-up, the evidence was downgraded to very low (once for risk of bias, once for unexplained inconsistency and once for imprecision as the 95% CI overlapped with the MCID value). The mean functional status score was 1.91 for corticosteroid injection, and 0.33 points worse (95% CI 0.40 better to 1.06 worse, 2 studies, 329 participants, I^2 = 89%) for those who were prescribed a splint (Analysis 2.2).

2) Overall improvement

De Moraes 2021 measured remission of nocturnal paraesthesias, and we used these data. Moderate-certainty evidence (downgraded once for risk of bias) indicates that corticosteroid injection probably results in a higher rate of remission from nocturnal paraesthesias both at short-term and long-term follow-up.

At short-term follow-up, 19 of 47 participants (40%) in the splinting group and 37 of 52 participants (71%) in the corticosteroid group had improved, corresponding to an RR of 0.57 (95% CI 0.39 to 0.84, 1 study, 99 participants; Analysis 2.3).

At long-term follow-up, 13 of 45 participants (29%) in the splinting group and 40 of 50 participants (80%) in the corticosteroid group had improved, corresponding to an RR of 0.36 (95% CI 0.22 to 0.58, 1 study, 95 participants; Analysis 2.3).

So 2018 reported median satisfaction score (0 to 5, higher is better). Median satisfaction was 3 (range 1-5) in the splinting group and 5 in the corticosteroid injection group.

3) Health-related quality of life

Chesterton 2018 measured this outcome by EQ-5D-5L (scale from 0 to 1, higher is better) and Taspinar 2007 by Health Assessment Questionnaire (scale from 0 to 3, higher is worse). For short-term follow-up, we rated the certainty of evidence as low (downgraded once for risk of bias and once for imprecision as the 95% CIs overlapped with the MCID value of 0.074 points). The SMD was -0.25 (95% CI -0.77 to 0.27, 2 studies, 270 participants, I^2 = 57%) favouring corticosteroid. This translates to 0.05 points worse in EQ-5D-5L (95% CI 0.15 worse to 0.05 better, MCID 0.074 points) for those prescribed a splint compared with corticosteroid injection (using an SD of 0.2 from Chesterton 2018) (Analysis 2.4).

At the long term, moderate-certainty evidence (downgraded once due to risk of bias) indicates that splinting probably does not improve health-related quality of life compared with corticosteroid injection. The mean EQ-5D-5L score was 0.82 in the corticosteroid group and 0.01 points better (95% CI 0.04 worse to 0.05 better, 1 study, 234 participants) for those prescribed a splint (Analysis 2.4 shows SMD due to several measures at the short term).

4) Adverse effects

Six studies reported adverse effects (Chesterton 2018; De Entrambasaguas 2006; De Moraes 2021; Sevim 2004; So 2018; Taspinar 2007). Reported adverse effects in the corticosteroid injection group were: skin changes (n = 4), hot flushes (n = 17), and short-lasting or long-lasting (over 3 days) pain (n = 53) (Chesterton 2018), vasovagal syncope (n = 1) (De Entrambasaguas 2006), short-lasting pain (n = 2) or small haematoma (n = 1) (Sevim 2004), short-lasting pain after the injection (n = 3) (So 2018), and increase in blood glucose level that required increasing the dose of oral antidiabetic drugs (n = 1) (Taspinar 2007). Adverse effects reported in the splinting group were discomfort (n = 11) (Chesterton 2018; So 2018) and allergic reaction on the skin (n = 1) (Sevim 2004).

We downgraded the evidence to very low (once for risk of bias, once for imprecision, and once for inconsistency).

- Chesterton 2018 reported 74 of 116 participants (64%) having adverse effects in the corticosteroid injection group versus 7 of 118 participants (6%) having adverse effects in the splinting group.
- De Entrambasaguas 2006 reported 1 of 24 participants (4%) having adverse effects in the corticosteroid injection group versus 0 of 26 participants (0%) having adverse effects in the splinting group.
- De Moraes 2021 reported zero adverse effects in both groups.
- Sevim 2004 reported 3 of 60 participants (5%) having adverse effects in the corticosteroid injection group versus 1 of 60 participants (2%) having adverse effects in the splinting group.
- So 2018 reported 3 of 25 participants (12%) having adverse effects in the corticosteroid injection group versus 4 of 25 participants (16%) having adverse effects in the splinting group.
- Taspinar 2007 reported 1 of 18 participants (5.5%) having adverse effects in the corticosteroid injection group versus 0 of 18 participants (0%) having adverse effects in the splinting group.

The pooled RR was 0.32 (95% CI 0.08 to 1.26, 6 studies, 590 participants, I^2 = 67%) (Analysis 2.5).

5) Referral for surgery

Chesterton 2018 reported this outcome at six weeks and at six months follow-up (in the analysis we included only the results from the 6 months follow-up) and De Moraes 2021 reported at six months.

The certainty of evidence was rated as very low (downgraded once for risk of bias and twice for serious imprecision). At six months, 15 of 166 participants (9%) in the splinting group were referred to surgery compared to 25 of 168 (15%) in the corticosteroid group, corresponding to an RR of 0.60 (95% CI 0.33 to 1.09, 2 studies, 334 participants, I^2 = 0%) (Analysis 2.6).

3. Splint versus oral steroid

One study (Mishra 2006) with 76 participants provided data for this comparison at one month and three months follow-up. We used the data from three months follow-up for short-term analysis. One study (Madjdinasab 2008) reported only electrophysiological outcomes and thus was not included in the meta-analysis.

Primary outcome: CTS symptoms

For short-term follow-up, low-certainty evidence (downgraded once for risk of bias and once for imprecision, as only one study with a low number of randomised participants, n = 76, contributed to the analysis) suggests that splinting and oral steroid may provide comparable benefits for improving symptoms. At short-term follow-up, the mean symptom severity score (measured by the BCTQ Symptom Severity Scale from 1 to 5 points, higher is worse, MCID value = 1 point) was 2.18 for those prescribed an oral steroid and 0.25 points worse (95% CI 0.03 better to 0.53 worse, 1 study, 71 participants) for those prescribed a splint (Analysis 3.1).

The only study in this comparison did not report this outcome at the long term.

Secondary outcomes

1) Function

For short-term follow-up, low-certainty evidence (downgraded once for risk of bias and once for imprecision, as only 1 study with a low number of randomised participants, n = 76, contributed to the analysis) indicated that hand function (measured by the BCTQ Functional Status Scale from 1 to 5, higher is worse, MCID = 0.7 points) may not differ between splinting and oral steroid use. The mean functional status score was 1.45 for those prescribed an oral steroid and 0.12 points worse (95% CI 0.06 better to 0.3 worse, 1 study, 71 participants) for those prescribed a splint (Analysis 3.2).

The only study in this comparison did not report this outcome at the long term.

2) Overall improvement

The only study in this comparison did not report this outcome.

3) Health-related quality of life

The only study in this comparison did not report this outcome.

4) Adverse effects

Mishra 2006 reported 2 of 36 participants (6%) having adverse effects in the splinting group (discomfort and swelling of the hand) and 0 of 35 participants (0%) having adverse effects in the oral steroid group. This corresponds to an RR of 4.86 (95% CI 0.24 to 97.86, 1 study, 71 participants). The evidence was downgraded to very low (once for risk of bias and twice for very serious imprecision) indicating that we are uncertain about the risk for adverse effects between these two treatments (Analysis 3.3).

5) Referral for surgery

The only study in this comparison did not report this outcome.

4. Splint plus corticosteroid injection versus corticosteroid injection

One study with 52 participants provided data for this comparison at six weeks and 12 weeks follow-up (Wang 2017). We used the data from 12 weeks follow-up for short-term analysis.

Primary outcome: CTS symptoms

For short-term follow-up, we graded the evidence as being of low certainty (downgraded once for risk of bias and once for imprecision, as only one study with a low number of participants, n = 52, contributed to the analysis). This evidence indicates that splinting given together with corticosteroid injection may not provide benefits in symptoms compared with corticosteroid injection alone. The mean symptom severity score (measured by the BCTQ Symptom Severity Scale from 1 to 5 points, higher is worse, MCID value = 1 point) was 1.49 with corticosteroid injection alone and 0.17 points better (95% CI 0.43 better to 0.09 worse, 1 study, 52 participants) with corticosteroid injection plus splint (Analysis 4.1).

The only study in this comparison did not report this outcome at the long term.

Secondary outcomes

1) Function

Low-certainty evidence (downgraded once for risk of bias and once for imprecision as only one study with a low number of participants, n = 52, contributed to the analysis) indicated that splinting given together with corticosteroid injection may not provide benefits in function compared with corticosteroid injection alone at short-term follow-up. The mean functional status score (measured by the BCTQ Functional Status Scale from 1 to 5 points, higher is worse, MCID value = 0.7 points) was 1.32 with corticosteroid alone and 0.05 points better (95% CI 0.28 better to 0.18 worse, 1 study, 52 participants) with corticosteroid injection plus splint (Analysis 4.2).

The only study in this comparison did not report this outcome at the long term.

2) Overall improvement

Low-certainty evidence (downgraded once for risk of bias and once for imprecision) indicated that splinting given together with corticosteroid injection may not result in higher rates of overall improvement compared with corticosteroid alone at short-term follow-up. In the splint plus corticosteroid injection group, 20 of 26 participants (77%) reported 'complete recovery' or 'much improved' (measured by a 6-point Likert-type scale) compared with 15 of 26 participants (58%) in the corticosteroid injection group alone. This corresponds to an RR of 1.33 (95% CI 0.90 to 1.97, 1 study, 52 participants) (Analysis 4.3).

The only study in this comparison did not report this outcome at the long term.

3) Health-related quality of life

The only study in this comparison did not measure this outcome.

4) Adverse effects

The only study in this comparison did not measure this outcome.

5) Referral for surgery

The only study in this comparison did not measure this outcome.

5. Splint versus exercise

One study (Schmid 2012) with 20 participants compared splinting with nerve and tendon gliding exercises at one week.

Primary outcome: CTS symptoms

Low-certainty evidence (downgraded once for risk of bias and once for imprecision as only one study with a low number of participants, n = 20, contributed to the analysis) indicates that the effect of splinting and nerve and tendon gliding exercises may not differ at short-term follow-up. The mean symptom severity score (measured by the BCTQ Symptom Severity Scale from 1 to 5 points, higher is worse, MCID value = 1 point) was 1.73 with exercises and 0.12 points worse (95% CI 0.38 better to 0.62 worse, 1 study, 20 participants) with splinting (Analysis 5.1).

The only study in this comparison did not measure this outcome at the long term.

Secondary outcomes

1) Function

Low-certainty evidence (downgraded once for risk of bias and once for imprecision as only 1 study with a low number of participants, n = 20, contributed to the analysis) indicates that function may not differ at the short term regardless of whether you are prescribed a splint or nerve and tendon gliding exercises. The mean functional status score (measured by the BCTQ Functional Status Score from 1 to 5 points, higher is worse, MCID value = 0.7 points) was 1.15 for those who were prescribed nerve and tendon gliding exercises, but was 0.30 points worse (95% CI 0.11 better to 0.71 worse, 1 study, 20 participants) for those who were prescribed a splint (Analysis 5.2).

The only study in this comparison did not measure this outcome at the long term.

2) Overall improvement

The only study in this comparison did not measure this outcome.

3) Health-related quality of life

The only study in this comparison did not measure this outcome.

4) Adverse effects

Schmid 2012 reported 0 of 10 participants (0%) having adverse effects in the splinting group and 0 of 10 participants (0%) having

adverse effects in the nerve and tendon gliding exercise group. Thus, we could not estimate the risk (very low-certainty evidence).

5) Referral for surgery

The only study in this comparison did not measure this outcome.

6. Stretching splint versus stretching exercises

One study with 50 participants compared Dynasplint (providing a low load transversal ligament stretching) with stretching exercises (Willis 2016).

Primary outcome: CTS symptoms

Willis 2016 reported symptom severity scores using an atypical scoring version of the BCTQ Symptom Severity Scale at short-term follow-up. According to the paper, the stretching splint (Dynasplint) group participants improved from 45.5 to 32.4 ($P < 0.001$) points, and in the stretching exercises group, the symptoms increased from 44.3 to 46.0 at two months.

The only study in this comparison did not measure symptoms at the long term.

Secondary outcomes

1) Function

The only study in this comparison did not measure this outcome.

2) Overall improvement

The only study in this comparison did not measure this outcome.

3) Health-related quality of life

The only study in this comparison did not measure this outcome.

4) Adverse effects

The only study in this comparison did not measure this outcome.

5) Referral for surgery

Low-certainty evidence (downgraded once for risk of bias and once for imprecision due to a low number of events) indicated that a stretching splint may decrease referral to surgery at one year. Willis 2016 reported that 7 of 25 participants (28%) had surgery in the stretching splint group and 16 of 25 participants (64%) in the stretching exercises group, corresponding to an RR of 0.44 (95% CI 0.22 to 0.88, 1 study, 50 participants) (Analysis 6.1).

7. Splint versus kinesiology taping

Primary outcome: CTS symptoms

Four studies) provided data for this outcome (Akturk 2018; Geler Kulcu 2016; Kocaoglu 2017; Oncu 2014). Akturk 2018 reported data at six weeks; Geler Kulcu 2016 reported data at four weeks; Kocaoglu 2017 reported data at three weeks; Oncu 2014 reported data at 25 days, two months and three months, from which we used the data from 25 days as it was the closest time point to the other studies in this comparison.

For short-term follow-up, low-certainty evidence (downgraded once for risk of bias, once for inconsistency and once for imprecision as the 95% CI overlapped with the MCID value) indicated that splinting may not improve symptoms compared with kinesiology taping. The 95% CI did not exclude a clinically important benefit for kinesiology taping up to three months after starting treatment. The mean symptom severity score (measured by the BCTQ Symptom Severity Scale from 1 to 5 points, higher is worse, MCID value = 1 point) was 2.05 with kinesiology taping and 0.49 points worse (95% CI 0.05 better to 1.03 points worse, 4 studies, 168 participants, I^2 = 78%) with a splint (Analysis 7.1).

None of the studies in this comparison reported this outcome at the long term.

Secondary outcomes

1) Function

Four studies (Akturk 2018; Geler Kulcu 2016; Kocaoglu 2017; Oncu 2014) provided data for this outcome. Akturk 2018 reported data at six weeks; Geler Kulcu 2016 reported data at four weeks; Kocaoglu 2017 reported data at three weeks; Oncu 2014 reported data at three months.

Low-certainty evidence (downgraded once for risk of bias, once for inconsistency and once for imprecision as the 95% CI overlapped with the MCID value) indicated that splinting and kinesiology taping may have comparable effects on hand function at short-term follow-up. The 95% CI did not exclude clinically important benefit for kinesiology taping. The mean functional status score (measured by the BCTQ Functional Status Scale from 1 to 5 points, higher is worse, MCID value = 0.7 points) was 1.72 for those prescribed kinesiology tape and 0.11 points worse (95% CI 0.54 better to 0.75 worse, 4 studies, 168 participants, I^2 = 79%) for those prescribed a splint (Analysis 7.2).

None of the studies in this comparison reported this outcome at the long term.

2) Overall improvement

None of the studies in this comparison reported this outcome.

3) Health-related quality of life

None of the studies in this comparison reported this outcome.

4) Adverse effects

None of the studies in this comparison reported this outcome.

5) Referral for surgery

None of the studies in this comparison reported this outcome.

8. Splint versus rigid tape

One study (Eraslan 2014) with 30 participants provided data for this comparison at three weeks.

Primary outcome: CTS symptoms

For short-term follow-up, low-certainty evidence (downgraded once for risk of bias and once for imprecision) suggests that rigid taping may slightly improve symptoms compared to night-time splinting but the 95% CI are consistent with both clinically important and unimportant benefit. The mean symptom severity score (measured by the BCTQ Symptom Severity Scale from 1 to 5 points, higher is worse, MCID value = 1 point) was 1.48 with rigid tape and 1.05 points worse (95% CI 0.58 worse to 1.52 worse, 1 study, 30 participants) with a splint (Analysis 8.1).

The only study in this comparison did not measure this outcome at the long term.

Secondary outcomes

1) Function

Low-certainty evidence (downgraded once for risk of bias and once for imprecision) suggests that hand function may be better after rigid taping compared with splinting at short-term follow-up. The 95% CIs excluded benefit for splinting. The mean functional status score (measured by the BCTQ Functional Status Scale from 1 to 5 points, higher is worse, MCID value = 0.7 points) was 1.71 for those prescribed rigid taping and 0.87 points worse (95% CI 0.48 worse to 1.26 worse, 1 study, 30 participants) for those prescribed a splint (Analysis 8.2).

The only study in this comparison did not measure this outcome at the long term.

2) Overall improvement

The only study in this comparison did not measure this outcome.

3) Health-related quality of life

The only study in this comparison did not measure this outcome.

4) Adverse effects

The only study in this comparison did not measure this outcome.

5) Referral for surgery

The only study in this comparison did not measure this outcome.

9. Splint versus platelet-rich plasma (PRP)

One study (Wu 2017) with 60 participants provided data for this comparison at one, three, and six months follow-up. We used the data from three months follow-up for short-term analysis.

Primary outcome: CTS symptoms

Low-certainty evidence (downgraded once for risk of bias and once for imprecision as only one study with a low number of participants, n = 60, contributed to the analysis) suggests the symptom improvement between splinting and PRP may be clinically unimportant both at the short term and long term.

At short-term follow-up, the mean symptom severity score (measured by the BCTQ Symptom Severity Scale from 1 to 5 points, higher is worse, MCID value = 1 point) was 1.43 for those who received PRP and 0.21 points worse (95% CI 0.01 worse to 0.41 worse, 1 study, 60 participants) for those prescribed a splint (Analysis 9.1).

At long-term follow-up, the mean symptom severity score was 1.29 for those who received PRP and 0.18 points worse (95% CI 0.01 worse to 0.35 worse, 1 study, 60 participants) for those prescribed a splint (Analysis 9.1).

Secondary outcomes

1) Function

Low-certainty evidence (downgraded once for risk of bias and once for imprecision as only one study with a low number of participants, n = 60, contributed to the analysis) suggests the difference between splinting and PRP is probably clinically unimportant in function both at the short term and long term.

At short-term follow-up, the mean functional status score (measured by the BCTQ Functional Status Scale from 1 to 5 points, higher is worse, MCID value = 0.7 points) was 1.35 with PRP and 0.35 points worse (95% CI 0.16 worse to 0.54 worse, 1 study, 60 participants) with a splint (Analysis 9.2).

At long-term follow-up, the mean functional status score was 1.30 with PRP and 0.32 points worse (95% CI 0.12 worse to 0.52 worse, 1 study, 60 participants) with a splint (Analysis 9.2).

2) Overall improvement

The only study in this comparison did not measure this outcome.

3) Health-related quality of life

The only study in this comparison did not measure this outcome.

4) Adverse effects

Wu 2017 reported 0 of 30 participants (0%) having adverse effects in the splinting group and 0 of 30 participants (0%) having adverse effects in the PRP group. Thus, we could not estimate the risk (very low-certainty evidence).

5) Referral for surgery

The only study in this comparison did not measure this outcome.

10. Splint versus extracorporeal shock wave therapy (ESWT)

One study (Ulucakoy 2020) with 83 participants provided data for this comparison. Results were measured at one month and three months follow-up. We used the data from three months follow-up for short-term analysis.

Primary outcome: CTS symptoms

Based upon moderate-certainty evidence (downgraded once for risk of bias), splinting probably does not improve symptoms compared with ESWT at short-term follow-up. The mean symptom severity score (measured by the BCTQ Symptom Severity Scale from 1 to 5 points, higher is worse, MCID value = 1 point) was 1.8 for those receiving ESWT and 0.1 points better (95% CI 0.40 better to 0.20 worse, 1 study, 83 participants) for those prescribed a splint (Analysis 10.1).

The only study in this comparison did not measure this outcome in the long term.

Secondary outcomes

1) Function

Moderate-certainty evidence (downgraded once for risk of bias) indicates that splinting probably does not improve function compared with ESWT at short-term follow-up. The mean functional status score (measured by the BCTQ Functional Status Scale from 1 to 5 points, higher is worse, MCID value = 0.7 points) was 1.9 with ESWT and 0.1 points better (95% CI 0.44 better to 0.24 worse, 1 study, 83 participants) for those prescribed a splint (Analysis 10.2).

The only study in this comparison did not measure this outcome at the long term.

2) Overall improvement

The only study in this comparison did not measure this outcome.

3) Health-related quality of life

The only study in this comparison did not measure this outcome.

4) Adverse effects

The only study in this comparison did not measure this outcome.

5) Referral for surgery

The only study in this comparison did not measure this outcome.

11. Dynamic splint plus rehabilitation versus rehabilitation

One study with 24 participants compared a dynamic splint (which allowed a limited range of motion from 15 degrees of flexion to 15 degrees of extension) plus rehabilitation (activity, ergonomic modifications, nerve and tendon gliding exercises, massage, carpal bones and nerve mobilisations, stretches of upper extremity and flexor retinaculum) with rehabilitation alone at six weeks (Jaladat 2017).

Primary outcome: CTS symptoms

Low-certainty evidence (downgraded once for risk of bias and once for imprecision as only one study with a low number of participants, n = 24 contributed to the analysis) indicates that dynamic splinting given together with rehabilitation may not improve symptoms compared with rehabilitation alone at short-term follow-up.

The mean symptom severity score (measured by the BCTQ Symptom Severity Scale from 1 to 5 points, higher is worse, MCID value = 1 point) was 2.25 with rehabilitation and 0.01 points worse (95% CI 0.61 better to 0.63 worse, 1 study, 24 participants) with splinting and rehabilitation (Analysis 11.1).

The only study in this comparison did not measure this outcome at the long term.

Secondary outcomes

1) Function

Low-certainty evidence (downgraded once for risk of bias and once for imprecision as only 1 one study with a low number of participants, n = 24, contributed to the analysis) indicates that dynamic splinting given together with rehabilitation may not improve function compared with rehabilitation alone. The mean functional status score (measured by the BCTQ Functional Status Scale from 1 to 5 points, higher is worse, MCID value = 0.7 points) was 1.9 with rehabilitation and 0.08 points better (95% CI 0.67 better to 0.51 worse, 1 study, 24 participants) with splinting and rehabilitation (Analysis 11.2).

The only study in this comparison did not measure this outcome at long-term follow-up.

2) Overall improvement

The only study in this comparison did not measure this outcome.

3) Health-related quality of life

The only study in this comparison did not measure this outcome.

4) Adverse effects

The only study in this comparison did not measure this outcome.

5) Referral to surgery

The only study in this comparison did not measure this outcome.

12. Splint six weeks versus splint 12 weeks

One study with 40 participants compared wearing a neutral wrist splint for six weeks to 12 weeks (Gatheridge 2020). The splint was worn at night primarily, but participants could wear the splint during the day (in addition to night-time) for activities that provoked symptoms.

Primary outcome: CTS symptoms

Low-certainty evidence (downgraded once for risk of bias and once for imprecision as only 1 study with a low number of participants, n = 37, contributed to the analysis) indicates that an additional six weeks splinting (6 versus 12 weeks) may not improve symptoms at short-term follow-up. At 12 weeks, the mean symptom severity score (measured by the BCTQ Symptom Severity Scale from 1 to 5 points, higher is worse, MCID value = 1 point) was 2.17 after 12 weeks of splinting and 0.18 points better (95% CI 0.62 better to 0.26 worse) with six weeks of splinting (Analysis 12.1).

The only study in this comparison did not measure this outcome at the long term.

Secondary outcomes

1) Function

Low-certainty evidence (downgraded once for risk of bias and once for imprecision as only 1 study with a low number of participants, n = 37, contributed to the analysis) indicates that an additional six weeks of splinting (6 versus 12 weeks) may not improve function beyond that achieved at six weeks total. At 12 weeks post-commencement of splinting, the BCTQ functional status score (measured by the BCTQ Functional Status Scale from 1 to 5 points, higher is worse, MCID value = 0.7 points) was 1.6 after 12 weeks of splinting and 0.05 points worse (95% CI 0.39 better to 0.49 worse) with six weeks splinting (Analysis 12.2).

The only study in this comparison did not measure this outcome at the long term.

2) Overall improvement

The only study in this comparison did not report this outcome.

3) Health-related quality of life

The only study in this comparison did not report this outcome.

4) Adverse effects

The only study in this comparison did not report this outcome.

5) Referral for surgery

Gatheridge 2020 reported this outcome at the long term, over three years. We downgraded the certainty of evidence to very low (once for risk of bias and twice for very serious imprecision as the 95% CIs included substantial effect in both directions). In the short-term splinting group, 2 of 17 participants (12%) had been referred to surgery compared to 4 of 20 participants (20%) in the long-term

splinting group corresponding to an RR of 0.59 (95% CI 0.12 to 2.83, 1 study, 37 participants; Analysis 12.3).

13. Splint six weeks versus splint six months

One study compared night-time splinting for six weeks with night-time splinting for six months (Sanaee 2017). Both groups also received usual care (non-steroidal anti-inflammatory drugs (NSAIDs), (naproxen 500 mg three times a day) for 10 days, vitamin B1 and B6 tabs for 6 weeks, physiotherapy (paraffin bath with controlled temperature, ultrasound underwater and grip exercises)). Outcomes were measured at six weeks and six months, but as both groups received exactly the same intervention for the first six weeks, we did not include the six weeks data in the analysis.

Primary outcome: CTS symptoms

At long-term follow-up, low-certainty evidence (downgraded once for risk of bias and once for imprecision as the 95% CI overlapped with the MCID value) indicates that six months of splinting may improve symptoms compared with six weeks of splinting. At six months, the mean symptom severity score (measured by the BCTQ Symptom Severity Scale from 1 to 5 points, higher is worse, MCID value = 1 point) was 2 with six months splinting and 1.3 points worse (95% CI 0.81 worse to 1.79 worse, 1 study, 156 participants) with six weeks of splinting (Analysis 13.1).

Secondary outcomes

1) Function

At long-term follow-up, moderate-certainty evidence (downgraded once for risk of bias) indicated that six months of splinting probably improves functional status compared with six weeks of splinting.

At six months, the mean functional status score (measured by the BCTQ Functional Status Scale from 1 to 5 points, higher is worse, MCID value = 0.7 points) was 1.8 with six months splinting and 2.3 points worse (95% CI 1.44 worse to 3.16 worse, 1 study, 156 participants) with six weeks of splinting (Analysis 13.2).

2) Overall improvement

The only study in this comparison did not report this outcome.

3) Health-related quality of life

The only study in this comparison did not report this outcome.

4) Adverse effects

The only study in this comparison did not report this outcome.

5) Referral for surgery

In the group that was prescribed a splint for six weeks, 4 of 59 participants (7%) had surgery versus 0 of 59 participants (0%) in the group that wore the splint for six months. This corresponds to an RR of 9.00 (95% CI 0.50 to 163.53, 1 study, 118 participants) (Analysis 13.3). We downgraded the certainty of evidence to very low (once for risk of bias and twice for very serious imprecision as the 95% CI included substantial effects in both directions).

14. Night-time splinting versus full-time splinting

One quasi-randomised trial with 24 participants compared night-time splinting versus full-time splinting for six weeks, at six weeks follow-up (Walker 2000).

Primary outcome: CTS symptoms

Low-certainty evidence (downgraded once for risk of bias and once for imprecision as only 1 study with a low number of participants, n = 26, contributed to the analysis) indicates that symptoms after six weeks night-time splinting and full-time splinting may not differ.

The mean symptom severity score (measured by the BCTQ Symptom Severity Scale from 1 to 5 points, higher is worse, MCID value = 1 point) was 2.3 with night-time splints and 0.21 points better (95% CI 0.83 better to 0.41 worse, 1 study, 24 participants) with full-time splinting (Analysis 14.1).

The only study in this comparison did not report this outcome at the long term.

Secondary outcomes

1) Function

Very low-certainty evidence (downgraded once for risk of bias and twice for imprecision; 1 study with 26 randomised participants and the 95% CI overlapping the MCID) indicates that we are uncertain about the effect on function after six weeks night-time splinting and full-time splinting.

At six weeks, the mean functional status score (measured by the BCTQ Functional Status Scale from 1 to 5 points, higher is worse, MCID value = 0.7 points) was 2.14 with night-time splinting and 0.21 points better (95% CI 0.87 better to 0.45 worse, 1 study, 24 participants) with full-time splinting (Analysis 14.2).

The only study in this comparison did not report this outcome at the long term.

2) Overall improvement

The only study in this comparison did not report this outcome.

3) Health-related quality of life

The only study in this comparison did not report this outcome.

4) Adverse effects

The only study in this comparison did not report this outcome.

5) Referral for surgery

The only study in this comparison did not report this outcome.

DISCUSSION

Summary of main results

The objective of this review was to assess the effects (benefits and harms) of splinting for people with carpal tunnel syndrome (CTS). We considered the results of 29 trials in a total of 1937 participants. Eight studies examined our primary comparison of splinting versus no treatment, 20 compared splinting with another non-surgical intervention (or splinting and a co-intervention compared to the same co-intervention). Three studies compared different splinting

regimens. Most of the participants were female (81 %). Participants had an average age ranging from 42 to 60 years.

Ten studies measured the effect of splint when delivered with some other non-surgical intervention: an exercise programme (Akturk 2018); a physical therapy programme (consisting of heat-application-ultrasound-TENS) and strengthening exercises (Eraslan 2014); usual rehabilitation including activity or ergonomic modifications, nerve- and tendon-gliding exercises, massage, carpal bones and nerve mobilisations, stretches of upper extremity and flexor retinaculum (Jaladat 2017); tendon and nerve-gliding exercises (Geler Kulcu 2016; Oncu 2014); corticosteroid injection (Wang 2017); nonsteroidal antiinflammatory drugs (NSAIDs), B_1 and B_6, paraffin bath, ultrasound underwater and grip exercise (Sanaee 2017); education (Hall 2013); and ergonomic education (Boonhong 2017; Werner 2005).

Splint versus no active treatment

For the primary outcome (symptoms), we found low-certainty evidence indicating that splinting may provide little or no benefit at short-term follow-up compared with no active treatment. The effect estimates excluded clinically relevant benefits, but there is no consensus on the ideal Minimal Clinically Important Difference (MCID) value in this specific context, and the chosen MCID value can affect interpretation (see Overall completeness and applicability of evidence). Regarding long-term follow-up (over 3 months), we are uncertain whether splinting provides benefit for CTS symptoms (Summary of findings 1).

Lack of blinding and heterogeneity in the treatment effects across the studies were the main limitations in the studies comparing splinting versus no active treatment at short-term follow-up. We explored heterogeneity by removing studies at high or unclear risk of selection bias. This left three small studies (i.e. Boonhong 2017; Geler Kulcu 2016; Oncu 2014) with low heterogeneity and moved the effect towards no effect, suggesting that the benefits observed in Manente 2001 and Premoselli 2006 may relate to shortcomings in the randomisation process.

On the other hand, the two studies reporting benefit for splint used splint only at night-time (Manente 2001; Premoselli 2006), and one study using night-time splint reported no benefit (Oncu 2014). The other trialists instructed participants to wear splints full time. Thus, inconsistency could also be partially explained by night-time splinting having a different effect compared with full-time use. However, one small study comparing night-time splinting with full-time splinting did not support this hypothesis (Walker 2000). Thus, it remains unclear if night-time splinting could improve symptoms, and if those benefits are present only at night-time or also at daytime, and if they are large enough to be important for people with CTS.

For secondary outcomes, moderate-certainty evidence suggested that splint probably does not improve hand function in the short term and may not improve hand function in the long term. Low-certainty evidence based upon one study suggested a benefit for splinting (RR of 3.9) in overall improvement (those reporting 'moderately' or 'much improved') (Manente 2001). This benefit was found in the study, which also reported benefits for CTS symptoms, unlike most studies. In this study, the first author reported owning the patent for the splint being tested. Therefore, we consider the evidence regarding benefits in overall improvement limited until confirmed in other studies.

None of the studies reported general health-related quality of life (HRQoL) in the primary comparison and the estimates were very imprecise for referral to surgery. We are thus uncertain about the effect of splinting for these outcomes.

Splinting may cause transient adverse effects (difficulty falling asleep and paraesthesia after removal). These adverse effects are generally minor and are not likely to persist after use is discontinued.

Other comparisons

The other comparisons supported the findings from the primary comparison. Splinting may not provide benefits in CTS symptoms or hand function when given together with corticosteroid injection (moderate-certainty evidence) or with rehabilitation (low-certainty evidence) nor when compared with corticosteroid (injection or oral; low certainty), exercises (low certainty), kinesiology taping (low certainty), rigid taping (low certainty), and probably does not improve outcomes compared with platelet-rich plasma (moderate certainty), or extracorporeal shock wave therapy (moderate certainty).

Splinting versus corticosteroid injection

Corticosteroid injections (when compared to splinting) appeared to provide a small, but clinically unimportant benefit in the short term with respect to symptom resolution (but not in improving function). However, this effect vanished at long-term follow-up, which is consistent with findings that the effect of corticosteroid injection is likely transient (Huisstede 2010). However, the results were inconsistent at long-term analysis. One study found that overall improvement (remission from nocturnal paraesthesias) was better with corticosteroid injection both at short- and long-term follow-up. With respect to health-related quality of life (HRQoL), corticosteroid injections and splint appeared to be comparable (low certainty), but the confidence intervals (CIs) did not exclude benefit for corticosteroid in the short term. Regarding harms, we did not find statistically significant differences in the reporting of adverse effects or in referral to surgery between the two treatments.

Comparison of splint wearing regimens

Regarding different splint-wearing regimens, one study found that six months of splinting may improve symptoms and function (low-certainty evidence) compared with six weeks splinting, suggesting that the benefits of splinting may manifest late (Sanaee 2017). Although the mean difference was at a clinically-relevant level, the 95% CI overlapped with the MCID value, and it is thus unclear if the effect is clinically relevant. When six weeks of splint use was compared with 12-week use, there was no evidence of benefit for a longer splinting period in symptoms or function (other outcomes were not measured).

Overall completeness and applicability of evidence

Participants in the studies had a typical age and sex distribution for people with CTS and the results are likely to be applicable to people with mild-to-moderate stages of the condition (Atroshi 1999; Concannon 2000; Jablecki 2002; Szabo 1994). Most studies excluded people with severe CTS and since the effect of splinting seems small at best, biological plausibility does not support the

hypothesis that splinting would benefit people with more severe symptoms, established axonal loss and subsequent permanent degenerative changes in the median nerve. However, no studies assessed effects in this population, probably because severe CTS is commonly considered an indication for surgery.

Some studies in the splinting versus no active treatment comparison provided education as a co-intervention (Boonhong 2017; Hall 2013; Werner 2005), or instruction for home-based exercises along with splinting and in the control group (Geler Kulcu 2016; Oncu 2014). Although education may improve coping and could impact the reported values, we deemed that these co-interventions were unlikely to bias the comparison as they were offered to participants in both groups. Furthermore, we can presume education to be present in normal clinical practice, including in studies that did not report it explicitly.

Regarding comparisons of splinting with other active non-surgical treatment modalities, since splinting has not shown efficacy compared with no splint, these studies provide little guidance whether splinting should be used or not. For this reason we excluded comparisons of specific splint designs. The observed changes in these studies may occur due to nonspecific effects and the between-group differences can be due to harms of the comparator. Although we excluded different splint designs from this update, they may be included in future updates if splinting shows clinically relevant efficacy. The major problem with these comparisons is the applicability of the evidence due to specificity of commercial or individually-tailored splints,

We could not identify an optimal splint-wearing regimen based on evidence from studies comparing different regimens. There was limited evidence from one study that the benefit may manifest late (Sanaee 2017), but no studies that compared splinting and no active treatment followed participants for more than six months in the primary analysis and, thus, it is still unclear if splinting can improve symptoms or other outcomes or decrease the need for surgery in long-term follow-up.

Another potentially important aspect of CTS that the trials did not specifically study was relief of night-time symptoms. In early CTS, people may suffer night-time symptoms almost exclusively. None of the studies specifically measured night-time symptom relief. Night-time symptoms comprise only 4/11 (36% weight) items in the BCTQ symptom severity score and patient-important benefits (e.g. better sleep and consequent improved daytime quality of life) may not be evident when BCTQ is used as the outcome measure for 'symptoms'.

We used CTS symptoms (a continuous outcome) as the primary outcome because very few studies measured global improvement (which was used in the previous update of this review as the primary outcome; Page 2012b) and we could not identify evidence suggesting that global improvement would be a clinically more relevant outcome. We excluded neurophysiological outcomes. Although they may be considered objective measures of improvement, their clinical relevance is unclear; if the possible benefit in conduction velocity does not translate to an improvement in symptoms, function, or health-related quality of life, it is not likely to be meaningful to people with CTS.

We did not include comparisons to surgery, as they are covered in another review (Verdugo 2008). We also excluded studies that compared splinting with a non-surgical intervention aimed at symptom modification. These interventions include electroacupuncture; yoga; gabapentin; flax seed oil; interferential current; or phonophoresis.

Quality of the evidence

None of the included studies was at low risk of bias. The main study limitation was lack of blinding (high risk of performance and detection bias). We identified one ongoing study using soft bandage as a placebo control (Atroshi 2019). Presumably soft bandage does not exert an effect, but nevertheless the participants were not blinded, and participant preconceptions can modify perceived improvement. It may not be feasible to create a placebo splint that achieves adequate blinding and does not exert any effect. Although meta-epidemiological studies indicate that a lack of blinding of participants or study personnel can affect estimates of effect (Savovic 2018), recent evidence suggests that this effect may be small (Moustgaard 2020). As bias from lack of blinding is likely to be context-dependent, it is unclear how much it can bias the estimates. We hypothesise that if splinting does not show a relevant effect in non-blinded trials, we should assume that blinded trials will find an even smaller effect.

We downgraded the evidence in the primary outcome for splint compared to no active treatment due to inconsistency. While two studies with high or unclear risk of selection bias reported statistically significant benefits for splinting, the studies at low risk of selection bias found a virtually null effect.

For function, the evidence was moderate (downgraded for risk of bias), the estimates excluding the MCID value. For overall improvement, we downgraded the certainty of evidence to low due to risk of bias and imprecision, as there was only one small study with 80 participants. Regarding harms, we downgraded the certainty of evidence for risk of bias (lack of blinding) and imprecision (the 95% CI included no effect).

Most secondary comparisons included one small unblinded study. Therefore, the estimates were often imprecise (moderate to low certainty of evidence, depending on the comparison and outcome).

Heterogeneity in the reported MCID values adds another layer of uncertainty to interpretation of the results. We used a MCID of 1 point (on a 1 to 5 scale) for BCTQ symptom severity score and 0.7 for BCTQ functional status score (Kim 2013), both from the mid-range of reported values (De Kleermaeker 2018). MCID values have often been defined in surgical studies, and may not apply directly to splinting. A MCID of 1 point is a relatively high value when translated to a standardised mean difference (SMD) (corresponds with large effect; SMD of 1.25 to 2). Although the chosen MCID value did not affect the estimates, a better understanding of what constitutes a meaningful change in people who use a splint would affect interpretation of results. For example, if we assume a MCID in the symptom scale that is 10% of the scale (0.4 points; corresponding with a medium to large effect, SMD of 0.6 to 1), our conclusions would be that splinting may provide clinically important benefits in carpal tunnel symptoms. However, inconsistency, imprecision and bias would still decrease our certainty, and more rigorous studies are needed.

Conflicts of interest were rarely reported: only two studies reported conflicts of interest that could affect the findings: one due to a

patent on the splint used in the trial (Manente 2001), and the other because two authors had been employed by the manufacturer of the tested stretching splint (Willis 2016).

Potential biases in the review process

We conducted searches according to Cochrane methodological standards and did not restrict searches by language or date. It is unlikely that we missed large-scale rigorous trials. However, based on clinical trial registries, we identified six potentially eligible studies that lacked the needed information or were not published, which are awaiting classification (Baklaci 2015; Bhuva 2019; IRCT2014020416485N1; ISRCTN22916517; Riasi 2015; Soon 2015). Inclusion of these trials could affect the estimates in this review.

Another study was included, but the authors did not report sufficient data to contribute to the analyses (Rioja Toro 2012).

Agreements and disagreements with other studies or reviews

The findings of this review are generally consistent with those of other systematic reviews of non-surgical interventions for CTS, which conclude that splinting may be more effective than no treatment, but is not more or less effective than other non-surgical interventions (Ashworth 2010; Gerritsen 2002b; Goodyear-Smith 2004; Huisstede 2010; Muller 2004; Ono 2010; Piazzini 2007).

Compared to the previous version of this review, we included 20 new studies, and we could pool more data in comparisons of splint versus no active intervention and splint versus corticosteroid. The findings largely agree with the previous version of the review regarding uncertainty of benefits, but we improved certainty regarding symptoms and function in the main analysis (increasing the certainty of evidence from very low to low certainty).

AUTHORS' CONCLUSIONS

Implications for practice

There is insufficient evidence to conclude whether wrist splinting provides clinically meaningful benefit for people with carpal tunnel syndrome (CTS). Current limited evidence does not exclude small improvements in CTS symptoms and hand function, but they may not be clinically important. However, the clinical relevance of small differences is still unclear and further research may change this conclusion. People may have greater chance of experiencing overall improvement when they use night-time splints compared with no splints.

Since splinting is a relatively inexpensive intervention with no plausible long-term harms, small effects (smaller than the MCID value) could justify use, particularly when people have mild-to-moderate CTS symptoms and are not interested in having surgery or injections.

It is still unclear if splint should be used full-time or at night-time only and whether long-term use is better than short-term use for best response. However, low-certainty evidence suggests that the benefits may manifest at long-term follow-up (after three months) and therefore longer treatment periods can be tried if the person with CTS does not develop adverse effects or worsening of symptoms.

Implications for research

As long as the efficacy of splinting is unclear, comparing splinting with other treatment modalities (often of ambiguous efficacy) may not improve our understanding of the role of splinting in the treatment of CTS. There is an apparent need for a large rigorous trial comparing splinting with no splinting or placebo and only one of the identified ongoing trials will address this research question (Atroshi 2019). Besides measuring improvement in symptoms and function, the trial authors should measure overall/global improvement, generic health-related quality of life, and record adverse effects and referral to surgery.

The trials should preferably have a long follow-up (and continue the intervention for 6 to 12 months or longer) to assess if any effects endure or manifest late. It may also be wise to further explore the optimal splinting strategy in terms of full-time versus night-time-only splinting – people with predominantly night-time symptoms may be a subgroup worth assessing separately, measuring specifically night-time symptom relief. Baseline symptom severity is a potential effect modifier and future studies could try to assess if there are subgroups of people that benefit more from splinting.

If participants with bilateral CTS are included in trials, trialists should use statistical methods which take the dependency between wrists into account, and report which statistical methods they used to achieve this. Lastly, MCID values in people undergoing splinting warrants further assessment, as this value can greatly impact the interpretation of the evidence.

ACKNOWLEDGEMENTS

We thank Ruth Brassington, Angela Gunn, and Farhad Shokraneh from the Cochrane Neuromuscular Disease Group for their assistance in database searches strategy, and ongoing support for this review. We thank Joona Juurakko for his help in data extraction.

We thank the peer reviewers for their helpful comments.

- Catrin Tudur Smith, University of Liverpool
- Janet Wale, independent patient advocate
- Pietro Caliandro Dipartimento di Scienze dell'Invecchiamento, Neurologiche, Ortopediche e della Testa-Collo, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
- Professor Richard Hughes, Emeritus Professor of Neurology, King's College London

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Akturk 2018

Study characteristics	
Methods	Study design: 2-arm assessor-blind RCT
	Setting: hospital physical therapy clinic in Turkey
Participants	**Details of sampling frame:**
	Total n eligible = not reported
	Total n excluded pre-randomisation = not reported
	Total n randomised = 58 hands (44 participants)
	Total n available for follow-up = 58 hands
	Total n analysed = 58 hands
	Intervention group 1 (splint + exercise) n = 30 hands
	Intervention group 2 (kinesiology tape + exercise) n = 28 hands
	Gender distribution:
	Total: 6 males; 38 females
	Intervention group 1 (splint + exercise): 1 male hand; 29 female hands

Akturk 2018 *(Continued)*

Intervention group 2 (kinesiology tape + exercise): 6 male hands; 22 female hands

Mean ± SD age:

Intervention group 1 (splint + exercise): 48.2 ± 9.2

Intervention group 2 (kinesiology tape + exercise): 49.2 ± 11.7

Total: aged 20–65 years

Mean ± SD duration of CTS symptoms:

Intervention group 1 (splint + exercise): 7.13 ± 1.96 weeks

Intervention group 2 (kinesiology tape + exercise): 7.6 ± 2.5 weeks

Inclusion criteria:

1. Pain or numbness spreading to the palmar face of the hand
2. At least one of the following positive in the physical examination: Tinel's sign, Phalen's test, or carpal compression tests
3. Symptoms for at least 3 months
4. An electrophysiological diagnosis of mild-to-moderate idiopathic CTS

Exclusion criteria:

1. Diabetes
2. Rheumatoid arthritis
3. Thyroid disease
4. Brachial plexopathy
5. Polyneuropathy
6. Cervical radiculopathy
7. Prior wrist fractures
8. Prior CTS surgery
9. Prior steroid injections to treat CTS

CTS diagnostic criteria (case definition):

People diagnosed with mild-to-moderate CTS by electroneuromyography (ENMG) were included in the study

CTS severity:

Mild-to-moderate idiopathic CTS

Interventions	Group 1: **treated with splinting**. Flexion, extension, and deviation of the wrist were not allowed in the splinted group but pronation and supination were. Neutral position, volar-assisted splints were applied and the participants were advised to wear them during the night-time and also at daytime whenever possible for 35 days. Participant comfort when wearing splint was checked on a weekly basis. Group 2: **kinesiology tape** was applied using the neural and inhibition techniques recommended for CTS. Alcohol-drenched cotton was used to clean the skin of oils and moisture with the wrist at 30° extension, the forearm in supination and the elbow in extension. For the neural technique, two 2.5 cm-wide strips were prepared by measuring the distance from the participant's first metacarpal joint to medial epicondyle. The 1st band for the median nerve was taped from 2nd and 3rd metacarpophalangeal joints to the medial epicondyle with medium stretch (60%) through the nerve trace. The 2nd strip was applied to the lateral epicondyle from the 4th and 5th metacarpophalangeal joints by applying the inhibition technique. A 3rd strip 4 cm wide was cut and applied to the volar face of the hand with full stretch. Taping was performed by the same physiotherapist twice a week for 5 weeks, 10 times in total. The tape was removed after 48 hours and reapplied after 24 hours of rest due to skin irritation. During this time, the participant was informed that he or she should not engage in activities that could cause excessive sweating and should not be exposed to water.

Akturk 2018 *(Continued)*

	Both groups: All participants were advised to report any discomfort when using the splint or kinesiology tape. The exercises for the tendons and nerve-shifting were written down and the participants were told to carry them out every day for 35 days. The**exercise programme** was given to all groups in the form of a home schedule and they were also given demonstrations. If symptoms were provoked during exercise, it was recommended to continue the exercise regimen using a smaller range of motion. Exercise compliance was monitored with a diary and checked on a weekly basis.
Outcomes	Outcomes evaluated before treatment and 6 weeks after treatment 1. BCTQ symptom severity score (1 to 5 higher is worse) 2. BCTQ functional status score (1 to 5 higher is worse) 3. DML (ms, higher is worse) 4. DSL (ms, higher is worse) 5. SNCV (m/s, higher is better) 6. Physical examination findings (positive provocative tests, sensory examination)
Funding	Not reported
COI	Not reported
Notes	BCTQ results reported as 10 to 50 in the table. Scale converted to 1 to 5 by dividing by 10. No information on whether the trial allowed participants to use other medication such as analgesic drugs or NSAIDs Exercise compliance was monitored with a diary and checked on a weekly basis, but nothing reported regarding the compliance with splint or kinesiology tape use. The results of compliance not provided

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was made by drawing lots".
Allocation concealment (selection bias)	Unclear risk	Quote: "Randomization was made by drawing lots". Comment: No information regarding the method of allocation was reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: blinding of participants not reported, but due to the nature of the interventions (splint versus taping), it is likely that participants were aware which treatment they were allocated to. Blinded observer is not adequate blinding regarding participant-reported outcome (BCTQ). Quote: "An observer who was blinded to the treatment method filled in an evaluation form both before treatment and in the sixth week following treatment."
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "An observer who was blinded to the treatment method filled in an evaluation form both before treatment and in the sixth week following treatment." Comment: Since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.
Incomplete outcome data (attrition bias)	Low risk	Comment: Not reported, probably no loss to follow-up

Akturk 2018 *(Continued)*
3 months or less

Selective reporting (reporting bias)	Unclear risk	Comment: All the outcomes specified in the methods reported, but no study protocol available, therefore, the risk was unclear.
Other bias	Unclear risk	Comment: 1) Trial reported BCTQ on a scale of 10 to 50, although normal range is from 1 to 5. As the values reported similarly in each treatment group, we transformed to values to 1 to 5, as this likely does not cause bias. 2) 14 participants had bilateral CTS. Clustering not controlled in the analyses; not clear if these 14 participants were distributed evenly 3) Gender distribution not balanced at baseline (29/30 women versus 22/28 women)

Boonhong 2017

Study characteristics	
Methods	Study design: 3-month randomised, single-blind, controlled trial Setting: outpatient unit and electrodiagnostic laboratory of the Department of Rehabilitation Medicine, King Chulalongkorn Memorial Hospital, Bangkok, Thailand
Participants	**Details of sampling frame:** Total n assessed for eligibility = 128 patients Total n excluded pre-randomisation = 74 patients Total n randomised = 54 participants (hands) Total n available for follow-up = 54 participants (hands) Total n analysed = 54 participants (hands) Intervention group 1 (splint) n = 28 participants (hands) Intervention group 2 (control) n = 26 participants (hands) **Gender distribution:** Intervention group 1 (splint): 1 male; 27 female Intervention group 2 (control): 3 male; 23 female **Mean ± SD age:** Intervention group 1 (splint): 53 ± 12.4 years Intervention group 2 (control): 53.6 ± 12.2 years **Mean ± SD duration of CTS symptoms:** Intervention group 1 (splint): 6.7 ± 6.6 months Intervention group 2 (control): 6.1 ± 6.6 months **Inclusion criteria:**

Boonhong 2017 *(Continued)*

1. Symptoms associated with CTS
2. Physical examination and unilateral or bilateral electrodiagnostic study
3. Mild-to-moderate CTS
4. Willing to join the study

Exclusion criteria:

1. CTS previously treated with steroid injection or surgery
2. History of hand or wrist injury
3. Diagnosed as cervical radiculopathy or peripheral neuropathy
4. Underlying disorders resulting from poorly controlled diabetes mellitus
5. Pregnancy
6. Other metabolic diseases
7. Exclude severe cases of CTS (CMAP amplitude less than 5.0 mV)

CTS diagnostic criteria (case definition):

Electrodiagnostic tests of sensory and motor nerve conduction were performed at baseline to confirm the diagnosis of mild to moderate CTS (to exclude severe cases of CTS (CMAP amplitude less than 5.0 mV) and other neurological conditions).

CTS severity:

Mild-to-moderate CTS

Interventions	Group 1 - **splinting group**: a commercially available adjustable wrist splint that was properly fitted and that immobilised the wrist in the neutral position. Participants were advised to wear the splint as often as possible during the daytime as well as night-time (during the 3-month duration of the study) to achieve the maximum effectiveness. Group 2 - **control group**: received only condition-related patient instructions and education pamphlet **Both groups**: Participants were given instruction regarding the nature of CTS and advised to avoid full extension and flexion of the wrist, reduce heavy work activities, and avoid repetitive movements. An education pamphlet was given to participants to learn more by themselves.
Outcomes	Outcomes were measured at baseline and at 3 months after the start of treatment 1. BCTQ symptom severity score (1 to 5 higher is worse) 2. BCTQ functional status score (1 to 5 higher is worse) 3. SDLs (ms) 4. DMLs (ms) 5. Mean time of splint use during treatment period 6. Adverse events
Funding	The authors gratefully acknowledge the Ratchadapiseksompoj Fund of the Faculty of Medicine, Chulalongkorn University for financial support. Grant number is RA 53/54(2).
COI	The authors had no conflict of interest to declare.
Notes	The article did not report the SD for duration of CTS symptoms but we calculated it from the P value. The article reported the BCTQ symptom severity and functional status as median (IQL 25, IQL 75). There was no explanation for IQL 25 and IQL 75 and we assumed they meant 25^{th} percentile and meant 75^{th} percentile, and calculated IQR and SD based on this assumption. The calculation gave reasonable SD values and the study did not get particularly high or low weight in the analysis. Participants were not allowed other medication, such as analgesic drugs or NSAIDs.

Boonhong 2017 *(Continued)*

	All participants in the splinting group reported being able to use their splint during both daytime and night-time. Mean duration of splint wear was 6.2 ± 2.5 hours/day (min = 2 hours, max = 11 hours) and 8.0 ± 2.0 hours/day (min = 4 hours, max = 11 hours) for daytime and night-time, respectively.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomized sequence was computer-generated with results sealed in opaque, tamper-proof, numbered envelopes."
Allocation concealment (selection bias)	Low risk	Quote: "The randomized sequence was computer-generated with results sealed in opaque, tamper-proof, numbered envelopes." Comment: No further elaboration of whether the concealment was ensured, but likely that it was
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "A well-trained assistant who was blinded to the patient treatments and was not involved in patients' treatment, explained the questionnaire to the participants without any guide and let them answer independently." Comment: However, splinting and no treatment/education are obviously different from each other, therefore unlikely that the participants were blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "All electrodiagnostic studies were conducted by an examiner who was blinded to the patient treatment groups." Comment: However, since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: All participants were accounted for; dropouts and attrition did not happen.
Selective reporting (reporting bias)	Unclear risk	Quote: "The protocol for this study has been approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand." Comment: All the outcomes specified in the methods reported, but study protocol was not available for reading, therefore the risk of bias was unclear.
Other bias	Low risk	Comment: No other risk of bias detected

Chesterton 2018

Study characteristics

Methods	Study design: pragmatic, 2-arm, parallel-group, open-label, RCT Setting: 25 primary and community musculoskeletal clinics and services in England
Participants	**Details of sampling frame:** Total n eligible = 405 (750 assessed for eligibility) Total n excluded pre-randomisation = 516 Total n randomised = 234 participants (hands)

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Intervention group (splint) n = 118 participants (hands)

Intervention group (steroid injection) n = 116 participants (hands)

Post-intervention follow-up at 6 weeks:

Total n available for follow-up (6 weeks) = 217 participants (hands)

Total n analysed (6 weeks) = 234 participants (hands)

Intervention group (splint) n = 109 participants (hands)

Intervention group (steroid injection) n = 108 participants (hands)

Post-intervention follow-up at 6 months:

Total n available for follow-up (6 months) = 192 participants (hands)

Total n analysed (6 months) = 234 participants (hands)

Intervention group (splint) n = 96 participants (hands)

Intervention group (steroid injection) n = 96 participants (hands)

Gender distribution:

Intervention group 1 (splint): 37 males; 81 females

Intervention group 2 (steroid injection): 43 male; 73 females

Mean ± SD age:

Intervention group 1 (splint): 52.2 ± 14.9 (median 50.00, IQR 40.75–64.25)

Intervention group 2 (steroid injection): 52.6 ± 17 (median 53.50, IQR 39.25–65.00)

Duration of CTS symptoms (number of participants):

Splint < 3 months: 17

Splint 3–6 months: 33

Splint 6 months to 1 year: 27

Splint > 1 year: 39

Splint missing: 2

Steroid injection < 3 months: 19

Steroid injection 3–6 months: 37

Steroid injection 6 months to 1 year: 22

Steroid injection > 1 year: 34

Steroid injection missing: 4

Inclusion criteria:

1. Aged 18 years or older

2. Presented with a new episode of primary idiopathic mild or moderate CTS, which had been present for longer than 6 weeks

Exclusion criteria:

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1. Severe CTS exhibiting constant wrist and hand (specifically palm, index, or middle finger, or thumb) pain, numbness or sensory loss in the wrist and hand (specifically palm, index, or middle finger, or thumb), or thenar muscle atrophy
2. Corticosteroid injection or night splint for CTS within the preceding 6 months
3. Previous surgery in the affected wrist, trauma to the affected hand requiring surgery, or immobilisation in the previous 12 months
4. Current or previous infection of the affected wrist, local or systemic sepsis or infection, or intercurrent illness
5. Pregnant or lactating
6. In receipt of anticoagulants
7. History of hypersensitivity to methylprednisolone acetate or any of its excipients
8. Allergic to any of the splint materials
9. History of drug or alcohol abuse
10. Undergoing ongoing litigation
11. Unable to complete self-report questionnaires written in English

CTS diagnostic criteria (case definition):

A general practitioner or trained clinician (physiotherapist or occupational therapist) made the clinical diagnosis, standardised on the basis of presenting symptoms, clinical history, and physical tests using criteria developed as part of a consensus survey of general practitioners from the UK Primary Care Rheumatology Society. Mild CTS was defined as intermittent paraesthesia in the distribution of the median nerve, and moderate as constant paraesthesia, and reversible numbness or pain of idiopathic nature.

CTS severity:

Mild-to-moderate CTS

Interventions	Group 1 - **night-resting splint** to be worn for 6 weeks: a Beta Wrist Brace, which immobilised the wrist in a neutral or slightly extended position (20° from neutral). The splint was fitted according to the size of the participant's hand and arm with standard splints of differing sizes. The treating clinician showed the participants how to fit and remove the wrist splint and gave them two Arthritis Research UK patient leaflets: CTS and splints for arthritis of the hand and wrist. The clinician instructed the participants to do gentle range-of-motion exercises when removing the splint to prevent stiffness and reinforced adherence by verbal instruction. Group 2 - **corticosteroid injection**: received one injection of 20 mg methylprednisolone acetate (as 20 mg of Depo-Medrone from 40 mg/mL; Pfizer) via a disposable needle (23 G or 25 G) and syringe which was inserted at the wrist between the proximal and distal wrist crease to infiltrate the carpal tunnel. We did not allow injections into the palm of the hand. Participants were treated by the diagnosing clinician who used a sterile no-touch technique without local anaesthetic. Participants were advised to wait for 30 min following injection and to rest the injected arm for 48 hours They were given 2 Arthritis Research UK patient leaflets for CTS and local corticosteroid injections. **Both groups**: no other types of therapy in either group were advised during the first 6 weeks, except for simple analgesia either prescribed or bought over the counter (paracetamol and NSAIDs).
Outcomes	Outcomes evaluated before, 6 weeks and 6 months after treatment; Secondary outcome measures at 6 weeks, 6 months, 12 months, and 24 months 1. BCTQ symptom severity score (1 to 5 higher is worse) 2. BCTQ functional status score (1 to 5 higher is worse) 3. BCTQ total score 4. Hand–wrist symptom intensity (0–10 numerical rating scale) 5. Referral for surgery 6. Surgery 7. Self-reported adherence 8. Secondary outcome measures at 6 weeks and 6 months only included interrupted sleep

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	9. Secondary measures at 6 months, 12 months, and 24 months only were over-the-counter and prescribed analgesia, perceived benefit and satisfaction with treatment, impact of CTS on work and activities, general health (EuroQoL EQ-5D-5L), healthcare use and patient-incurred costs, and use of co-interventions 10. Performance at work and days off work 11. Serious or unexpected adverse events
Funding	"This paper presents independent research funded by an Arthritis Research UK grant (Grant Number 20105). EMH is a National Institute for Health Research (NIHR) senior investigator. KSD is part-funded by a Knowledge Mobilisation Research Fellowship (KMRF-2014-03-002) from the NIHR and the NIHR Collaborations for Leadership in Applied Health Research and Care West Midlands. The views expressed in this paper are those of the author(s) and not necessarily those of the National Health Service, the NIHR, or the Department of Health and Social Care."
COI	The authors declared no competing interests.
Notes	Even though there was a dropout of participants at 6 weeks and 6 months, analyses were based on multiple imputed data. Participants with bilateral CTS were permitted treatment for the non-study hand according to normal clinical protocols in use at the research site. Some participants were diagnosed with hypothyroidism and diabetes. 5/234 had had surgery for CTS. Outcomes were not reported for this subcohort separately, so we could not exclude these participants. As the proportion was low, we did not exclude this study. In the corticosteroid injection group, 3 participants either received an incorrect injection (n = 2) or additionally to the injection wore a night splint (n = 1). In the night splint group, 28 participants either received a corticosteroid injection in addition to the night splint (n = 2), wore the splint on the wrong hand (n = 3), did not wear the splint for at least 4–6 nights per week (n = 4), or did not provide adherence data (n = 19).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants were randomly assigned (1:1) to either treatment group with permutated blocks of sizes two and four, prestratified by research site. Randomisation was completed by the Keele University (Keele, UK) Clinical Trial Unit's (CTU) online web or telephone randomisation service."
Allocation concealment (selection bias)	Low risk	Quote: "Randomisation was completed by the Keele University (Keele, UK) Clinical Trial Unit's (CTU) online web or telephone randomisation service. The allocation sequence was not available to research team members. We could not mask treating clinicians or patients to treatment allocation, but we concealed the treatment group allocation during the analyses. A letter was sent to the GPs (general practitioners) of all participants informing them of their patient's participation in the trial and their treatment allocation."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "We could not mask treating clinicians or patients to treatment allocation, but we concealed the treatment group allocation during the analyses."
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "We could not mask treating clinicians or patients to treatment allocation, but we concealed the treatment group allocation during the analyses."

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Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: All participants were accounted for and reasons for dropouts and attrition were documented (9/118 versus 8/116 missing data at 6 weeks and 20/118 versus 20/118 at 6 months: balanced loss). Authors also did per protocol sensitivity analysis (for 28/118 versus 3/116 participants treatment deviated from protocol).
Incomplete outcome data (attrition bias) After 3 months	Low risk	Comment: All participants were accounted for and reasons for dropouts and attrition were documented (9/118 versus 8/116 missing data at 6 weeks and 20/118 versus 20/118 at 6 months: balanced loss). Authors also did per protocol sensitivity analysis (for 28/118 versus 3/116 participants treatment deviated from protocol).
Selective reporting (reporting bias)	Unclear risk	Comment: Protocol available. Perceived benefit and satisfaction with treatment seems not to be reported, but since this was a secondary outcome, it was not clear if non-reporting was related to the nature of the findings.
Other bias	Low risk	Comment: No other risk of bias detected

De Entrambasaguas 2006

Study characteristics	
Methods	Study design: Randomised, single-blind, controlled trial Setting: general university hospital, Spain. Study population included people referred to the clinical neurophysiology service.
Participants	**Details of sampling frame:** Total n eligible = 88 wrists Total n excluded pre-randomisation = 13 wrists Total n randomised = 75 wrists Intervention group 1 (splint) n = 26 wrists Intervention group 2 (steroid injection) n = 24 wrists Intervention group 3 (phonophoresis) n = 25 wrists Post-intervention follow-up: Total n available for follow-up = 38 participants (52 wrists) Total n analysed = 52 wrists Intervention group 1 (splint) n = 18 wrists Intervention group 2 (steroid injection) n = 18 wrists Intervention group 3 (phonophoresis) n = 16 wrists **Gender distribution:** Total: 8 male wrists, 44 female wrists (n of participants not reported) Intervention group 1 (splint): 0 male wrists, 18 female wrists

De Entrambasaguas 2006 *(Continued)*

	Intervention group 2 (steroid injection): 6 male wrists, 12 female wrists Intervention group 3 (phonophoresis): 2 male wrists, 14 female wrists **Mean ± SD (range) age:** Intervention group 1 (splint): 50 ± 10.7 years Intervention group 2 (steroid injection): 45.4 ± 7.8 years Intervention group 3 (phonophoresis): 58.2 ± 8.1 years Total: 50.7 ± 10.3 (25 to 73) **Mean ± SD (range) duration of CTS symptoms:** Total: 10.7 ± 20.5 (2–80) months **Inclusion criteria:** Mild CTS (increase of sensory or mixed latencies of the median nerve, regardless of the amplitude of potentials) or moderate CTS (criteria for mild CTS plus increase of DML of the median nerve) **Exclusion criteria:** 1. Severe CTS (absence or low amplitude of sensory or motor potentials, with presence of denervation or reinnervation on needle EMG) 2. CTS previously treated, surgically or otherwise 3. Presence of any condition aetiologically related to CTS, with the exception of manual work 4. Treatment being carried out at the time for whatever reason with anti-inflammatory drugs **CTS diagnostic criteria (case definition):** Clinical suspicion of CTS was confirmed by means of electromyographic studies (EMG). **CTS severity:** Mild and moderate CTS
Interventions	Group 1: **splinting** – each splint was modelled individually for each hand, and worn for 12 hours daily for four weeks; if uncomfortable, splint was adjusted. Group 2: **steroid injection** - injection of 40 mg of triamcinolone with 10 mg of lidocaine Group 3: phonophoresis - diclofenac gel was used to administer ultrasound pulses in 10-minute sessions, 5 days per week, for 4 weeks.
Outcomes	Outcomes assessed at baseline and 1 month after treatment ended: 1. Sensory symptoms: tingling, numbness, pain, autonomic manifestations (sweating of palms, changes in skin colour, subjective swelling or clumsiness) measured as 'better', 'worse' or 'no change' 2. Physical examination: pinprick: median territory versus ulnar, abductor pollicis brevis muscle versus abductor digiti minimi, Tinel's sign at the wrist. Each measured as 'better', 'worse', or 'no change' 3. Nerve conduction: SDL of median nerve (third digit-wrist, longest), mixed median nerve (palm-wrist, shortest)
Funding	Not reported
COI	The authors declared that they had no conflict of interest.
Notes	Written in Spanish No treatment had side effects, except 1 participant had vasovagal syncope due to the emotional stress of the injection.

De Entrambasaguas 2006 *(Continued)*

As the number of participants (in addition to wrists) was available only for those who completed the study, we used this number when describing results.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: No information regarding how the random sequence was generated was reported.
Allocation concealment (selection bias)	Unclear risk	Comment: No information regarding the method of allocation was reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote from translation: "The patients were followed up one month after the end of the given treatment. It consisted of a new clinical evaluation, physical examination and EMG studies, identical to the initial protocol. This evaluation was made single-blind by the same physician who carried out the first study." Comment: The authors reported that personnel were blinded; however, the participants were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote from translation: "The patients were followed up one month after the end of the given treatment. It consisted of a new clinical evaluation, physical examination and EMG studies, identical to the initial protocol. This evaluation was made single-blind by the same physician who carried out the first study." Comment: The authors reported that personnel were blinded; however, the participants were not blinded.
Incomplete outcome data (attrition bias) 3 months or less	High risk	Comment: A flow chart detailed the number of wrists assigned to each group, plus the number of wrists in each group where participants rejected treatment, did not show up, or were excluded because follow-up was carried out by physicians not directly involved in the study, or because participants did not follow instructions. Loss to follow-up and reasons for these losses were not equally balanced across the groups.
Selective reporting (reporting bias)	Unclear risk	Comment: According to the translator, all outcomes reported in the Methods section were fully reported in the Results section of the report; however, the study protocol was not available.
Other bias	Unclear risk	Not clear how people with bilateral CTS were distributed

De Moraes 2021

Study characteristics

Methods	Study design: randomised, parallel-group, single (investigator)-blinded controlled trial Setting: hand surgery and microsurgery section of Hospital Alvorada, Américas, São Paulo/SP
Participants	**Details of sampling frame:** Total n eligible = not reported Total n excluded pre-randomisation = not reported Total n randomised = 100 participants (hands)

De Moraes 2021 *(Continued)*

Intervention group 1 (splint) n = 48 participants (hands)

Intervention group 2 (steroid injection) n = 52 participants (hands)

Post-intervention follow-up at 3 months:

Total n available for follow-up (3 months) = 99 participants (hands)

Total n analysed (3 months) = 99 participants (hands)

Intervention group (splint) n = 47 participants (hands)

Intervention group (steroid injection) n = 52 participants (hands)

Post-intervention follow-up at 6 months:

Total n available for follow-up (6 months) = 95 participants (hands)

Total n analysed (6 months) = 95 participants (hands)

Intervention group (splint) n = 45 participants (hands)

Intervention group (steroid injection) n = 50 participants (hands)

Gender:

Intervention group 1 (splint): 7 males; 41 females

Intervention group 2 (steroid injection): 10 males; 42 females

Mean age:

Intervention group 1 (splint): 54.4 years (SD not reported)

Intervention group 2 (steroid injection): 54.2 years (SD not reported)

Duration of CTS symptoms:

Inclusion criteria

1. Adults aged 40 years or more
2. Diagnosis confirmed with EMG
3. Four or more of the following six clinical signs and symptoms suggested by Graham and colleagues (Graham 2006) (CTS-6):
   a. Paraesthesia in the territory of the median nerve
   b. Hand paraesthesia at night
   c. Atrophy of thenar muscles
   d. Positive Tinel's sign
   e. Phalen's test positive
   f. Loss of 2-point discrimination (> 6 mm)
4. Signed informed consent
5. Symptoms for at least 1 month
6. A positive nerve conduction study indicating motor and sensory involvement, classified as moderate or severe

Exclusion criteria

1. Pretreatment with corticosteroids and splint within last 6 months
2. Prior surgical treatment for CTS
3. Wrist conditions associated with trauma
4. Non-trauma-associated conditions (cervical pain, shoulder girdle pain [chosen to rule out thoracic outlet syndrome], long-term uncontrolled diabetes)
5. Hypersensitivity or allergy to corticosteroids

De Moraes 2021 *(Continued)*

	6. Presence of persistent paraesthesia in the median nerve territory (radial fingers) 7. Refusal to participate **CTS diagnostic criteria (case definition):** A CTS diagnosis was made clinically and supported by electrodiagnostic findings. **CTS severity:** Moderate to severe CTS
Interventions	Group 1 - **a forearm-palmar orthosis** with the wrist immobilised in a neutral position was used at night while sleeping and removed in the morning. The duration of orthosis use differed because sleeping times were different between individuals. The orthosis was used throughout the study period. Group 2 - **corticosteroid injection**: 6.43 mg (1 mL) of betamethasone dipropionate, 2.63 mg of betamethasone disodium phosphate, and 0.5 mL of 2% lidocaine (xylocaine), totaling 1.5 mL. After injection, a simple dressing was applied.
Outcomes	Outcomes evaluated at baseline and after treatment (within the 1st week of the intervention, and 1, 3, and 6 months). 1. Remission of nocturnal paraesthesia 2. BCTQ symptom severity score (1 to 5; higher is worse) 3. BCTQ functional status score (1 to 5; higher is worse) 4. Pain (VAS, 10 cm line; higher is worse) 5. Adverse effects 6. Failure (worsening of, or no improvement in, CTS-related signs and symptoms, therefore requiring another therapeutic intervention)
Funding	None declared
COI	None declared
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The randomization procedure was performed by a person not directly involved in the study." Comment: Random sequence generation, however, not described
Allocation concealment (selection bias)	Low risk	Quote: "The allocation of patients was performed using opaque envelopes with consecutive numbers. Envelopes were only opened after verification of inclusion criteria and signing of the informed consent form. The randomization procedure was performed by a person not directly involved in the study." Comment: Adequate allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Outcome assessments were performed by blinded researchers." Comment: The participants were not blinded, and outcomes were partially or completely participant-reported.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Outcome assessments were performed by blinded researchers."

De Moraes 2021 *(Continued)*

		Comment: The participants were not blinded, and outcomes were partially or completely participant-reported.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Quote: "There was an overall loss to follow-up of 5 patients (5%). In the orthosis group, 1 patient did not return in the third month of follow-up, and another 2 were lost in the sixth month (6.25%). In the corticosteroid group, 2 patients (3.8%) did not return in the sixth month assessment." Comment: Small and balanced loss, and reasons reported. Not likely to bias outcomes considerably
Incomplete outcome data (attrition bias) After 3 months	Low risk	Small and balanced loss, and reasons reported. Not likely to bias outcomes considerably
Selective reporting (reporting bias)	Low risk	Main outcomes defined in the registration were reported. Graham criteria were defined as an outcome in the ClinicalTrials registry but not reported. This likely does not bias the results, as we did not consider those criteria as relevant in this review.
Other bias	Low risk	Randomisation and outcome measurement were performed at participant level. No other risk of bias detected

Eraslan 2014

Study characteristics	
Methods	**Study design:** 2-arm quasi-randomised trial **Setting**: unclear
Participants	**Details of sampling frame:** Total n eligible = not reported Total n excluded pre-randomisation = not reported Total n randomised = 30 participants (47 wrists) Total n available for follow-up = 30 Total n analysed = 30 Intervention group 1 (splint) n = 15 Intervention group 2 rigid taping) = 15 **Gender distribution** Intervention group 1 (splint): 2 male, 13 females Intervention group 2 (rigid taping): 2 male, 13 females **Mean ± SD (range) age:** Intervention group 1 (splint): 43.5 ± 13 Intervention group 2 (rigid taping): 48.9 ± 12 Total mean: 46.2 (aged between 21 and 71 years)

Eraslan 2014 *(Continued)*

	Mean ± SD (range) duration of symptoms, months Not reported **Inclusion criteria:** CTS according to the electroneuromyography (ENMG) and American Association of Electrodiagnostic Medicine criteria **Exclusion criteria:** 1. Trauma history like distal radius fracture 2. Connective tissue diseases 3. Malign tumours 4. Cervical degenerative disc diseases and fibromyalgia 5. People with CTS according to ENMG but having negative Tinel's sign and Phalen's test **CTS diagnostic criteria (case definition):** Not reported **CTS severity:** Not reported **Protocol violators:** None
Interventions	Group 1 - **splint**: On the 6th day of the treatment, participants were recommended night splint without thumb support. While allowing pronation and supination of the wrist, a neutral positioned splint with volar support was used, which would not allow flexion, extension and deviation. The participants were advised to use their splints for an average of 8 hours each night. Group 2 - **rigid taping**: Rigid taping was applied by stretching the carpometacarpal joint with the anchor tie around the thumb, relaxing the flexor retinaculum, and finally stretching the metacarpophalangeal joint and closing it with the last anchor tie on the thumb. **Both groups**: physical therapy programme consisting of 21 sessions of hot application-ultrasound-TENS. Hot application for 20 minutes, ultrasound for 4 minutes (1.5 W/cm^2 for 2 minutes in each hand), and 20 minutes of TENS (continuous mode) were applied once a day, 6 sessions a week. In the first 6 days of treatment, the participants were recommended to restrict excessive hand and wrist activities. On the 6th day of the treatment, both groups were given tendon shifting, median nerve shifting, strengthening exercises for the wrist, strengthening exercises for the intrinsic muscles, especially strengthening and stretching exercises for the thumb (abductor pollicis muscle) and median nerve stretching.
Outcomes	Outcomes were collected at baseline and at the 21st day of the treatment 1. BCTQ symptom severity score (1 to 5; higher is worse) 2. BCTQ functional status score (1 to 5; higher is worse) 3. VAS for pain at rest, activity and night (0 to 10; higher score indicates more pain) 4. VAS for paraesthesia (0 to 10; higher score indicates more paraesthesia)
Funding	Not reported
COI	Not reported
Notes	Article in Turkish, translation used

Eraslan 2014 *(Continued)*

	Results from BCTQ not reported in scale 1 to 5. We assumed that total sum was reported and divided symptom score by 11 and functional score by 8 (as per instructions of the scale).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote from translation: "Patients were allocated to two treatment groups as night splint and rigid taping. The first patient assigned to a group according to the coin toss method. The following patients were grouped considering the arrival order." Comment: Only the first participant was randomised and the rest were sequentially allocated, which is not true randomisation.
Allocation concealment (selection bias)	High risk	Quote from translation: "Patients were allocated to two treatment groups as night splint and rigid taping. The first patient assigned to a group according to the coin toss method. The following patients were grouped considering the arrival order." Comment: No true randomisation and the sequence was not concealed from the investigators.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Not reported, but due to the nature of the interventions (splint versus taping), it is likely that participants were aware of their allocated treatment.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: Data given for all participants in the table
Selective reporting (reporting bias)	Unclear risk	Comment: No protocol available to confirm the planned outcomes, therefore the risk was unclear. BCTQ reported fully for both groups
Other bias	Low risk	Comment: 1) The BCTQ scores were reported in a modified way. The standard method is to divide by the number of questions (scale 1 to 5) but the authors reported the total score (scale probably 19 to 95). However, this did not cause bias because both groups were reported similarly. 2) The level of analysis was the participant, therefore clustering should not affect the analysis.

Gatheridge 2020

Study characteristics

Methods	Study design: prospective, unblinded, randomised clinical trial with 12-week follow-up Setting: United States Air Force Academy
Participants	**Details of sampling frame:** Total n eligible = not reported Total n excluded pre-randomisation = not reported

Gatheridge 2020 *(Continued)*

Total n randomised = 31 (38 hands)

Intervention group 1 (splint 6 weeks) = not reported

Intervention group 2 (splint 12 weeks) = not reported

Post-intervention follow-up:

Total n available for follow-up = 30 (37 hands)

Total n analysed = 30 (37 hands)

Intervention group 1 (splint 6 weeks) = 14 (17 hands)

Intervention group 2 (splint 12 weeks) = 16 (20 hands)

Gender distribution:

Intervention group 1 (splint 6 weeks): 4 males; 10 females

Intervention group 2 (splint 12 weeks): 6 male; 10 females

Mean ± SD age:

Intervention group 1 (splint 6 weeks): 46.8 ± 6.35 (range 34–61)

Intervention group 2 (splint 12 weeks): 47 ± 6.35 (range 26–72)

Mean ± SD duration of CTS symptoms:

Intervention group 1 (splint 6 weeks): 51.2 ± 15.17 (range 12–156) weeks

Intervention group 2 (splint 12 weeks): 61.4 ± 15.17 (range 6–520) weeks

Inclusion criteria:

1. 18 years or older
2. Confirmed on routine electrodiagnostic study to have unilateral or bilateral mild or mild to moderate CTS
3. No prior treatment for CTS on the affected hand(s)
4. No prior use of wrist splint, corticosteroid injection, carpal tunnel release, acupuncture, physical or occupational therapy, or prescribed anti-inflammatory medication for their current symptoms

Exclusion criteria:

1. Prior wrist or hand surgery on the symptomatic side (even if unrelated to carpal tunnel symptoms)
2. Evidence of other mononeuropathy or cervical radiculopathy identified by electrodiagnostic study on the symptomatic side
3. Known pregnancy
4. Diagnosis of rheumatological disease or fibromyalgia

CTS diagnostic criteria (case definition):

Electrodiagnostic testing (to confirm having unilateral or bilateral mild or mild to moderate CTS)

CTS severity:

Mild-to-moderate CTS

Interventions	Group 1: **neutral wrist splint for 6 weeks** Group 2: **neutral wrist splint for 12 weeks** All participants were fitted with the Hely & Weber Titan Wrist Lacing Orthosis by manufacturer instructions in a wrist neutral position, where the wrist is in straight alignment with the forearm, limiting pres-

Gatheridge 2020 *(Continued)*

	sure on the carpal tunnel space. All participants received the same instruction for wearing the wrist splint, to include wearing the wrist splint every night for the specified duration. Participants were advised that they could wear the splint during the day (in addition to night-time) for activities that provoked symptoms; however, they were encouraged to attempt nocturnal splinting first. Participants were not given any work or activity restrictions.
Outcomes	Outcomes were assessed at baseline, 6 and 12 weeks 1. BCTQ symptom severity score (1 to 5 higher is worse) 2. BCTQ functional status score (1 to 5 higher is worse) 3. Compliance score (1-5, 1 = never) 4. Median DML (ms) 5. Median SDL (ms)
Funding	Not reported
COI	Not reported
Notes	SD value for age and duration of symptoms not reported in the article, but we calculated it from P value. At 6 and 12 weeks, participants were asked about their wrist splint compliance and, in a separate unvalidated survey, if they minded wearing the wrist splint. At 6 weeks, compliance was similar for both groups (P = 0.856). A total of 47% of the cohort reported wearing their wrist splint every night, and 91% reported wearing it for at least 5 to 7 nights. In weeks 6 to 12, 84% of participants in group 2 continued to wear the splint more than 5 nights. The majority of participants in group 1 did not wear the wrist splint (P = 0.004) during this time. 4 participants (5 hands) in group 1 reported that they did continue to wear the wrist splint, 2 wearing the splint frequently (5–7 nights).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Subjects were randomized to wear the wrist splint for either 6 weeks (group A) or 12 weeks (group B) by random block permutation, for which the PI was blinded". Comment: No further description how randomisation was achieved
Allocation concealment (selection bias)	Low risk	Quote: "Subjects were randomized to wear the wrist splint for either 6 weeks (group A) or 12 weeks (group B) by random block permutation, for which the PI was blinded. Once the subject was enrolled, the PI and subjects were unblinded to that subjects' splint use duration." Comment: No further information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Once the subject was enrolled, the PI [principal investigator] and subjects were unblinded to that subject's splint use duration."
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Once the subject was enrolled, the PI and subjects were unblinded to that subject's splint use duration."
Incomplete outcome data (attrition bias)	Low risk	The dropouts documented and reasons provided

Gatheridge 2020 *(Continued)*
3 months or less

Selective reporting (reporting bias)	Unclear risk	Comment: All outcomes specified in the methods were reported, but no study protocol was available, therefore the risk of bias is unclear.
Other bias	Unclear risk	Comment: 30 participants, 38 hands in the study. Clustering not controlled for. Bilateral condition in 3 versus 4 participants in the groups. Unclear if this could bias the comparison.

Geler Kulcu 2016

Study characteristics	
Methods	Study design: Randomised 3-arm, sham-controlled trial Setting: Turkey
Participants	**Details of sampling frame:** Total n assessed for eligibility = 57 Total n excluded pre-randomisation = 12 Total n randomised = 45 participants (65 wrists) Intervention group 1 (splint) n = 15 (21 wrists) Intervention group 2 (kinesiology tape) n = 15 (22 wrists) Intervention group 3 (placebo kinesiology tape) n = 15 (22 wrists) Post-intervention follow-up at 4 weeks: Total n available for follow-up = 40 participants (60 wrists) Intervention group 1 (splint) n = 14 (20 wrists) Intervention group 2 (kinesiology tape) n = 13 (20 wrists) Intervention group 3 (placebo kinesiology tape) n = 13 (20 wrists) **Gender distribution** Intervention group 1 (splint): 1 male; 13 females Intervention group 2 (kinesiology tape): 1 males; 12 females Intervention group 3 (placebo kinesiology tape): 0 males; 13 females **Mean ± SD age:** Intervention group 1 (splint): 51.3 ± 8.3 (range 40–65) Intervention group 2 (kinesiology tape): 49.8 ±11.5 (range 20–62) Intervention group 3 (placebo kinesiology tape): 48.95 ± 6.0 (range 40–60) Total: 50.02 ± 8.79 (20–65) years **Mean ± SD (range) duration of CTS symptoms** Not reported. All had CTS < 1 year **Inclusion criteria** 1. Mild-to-moderate CTS according to a nerve conduction study 2. 18 years or older 3. Symptoms for less than 1 year **Exclusion criteria** 1. Secondary entrapment neuropathy (e.g. diabetes, inflammatory arthritis, hypothyroidism, previous wrist trauma) 2. Pregnancy 3. Skin infection on the forearm

Geler Kulcu 2016 *(Continued)*

4. Cervical radiculopathy
5. Polyneuropathy
6. History of previous carpal tunnel decompression surgery
7. Previous history of a corticosteroid injection into the carpal tunnel

CTS diagnostic criteria (case definition):

1. People diagnosed by EMG as having mild to moderate CTS (according to NCSs)

CTS severity:

Mild-to-moderate CTS

Interventions	Group 1 - **wrist orthosis**: Participants were applied with a custom-made volar thermoplastic wrist orthotic device in a neutral wrist position. The participants were encouraged to use the orthosis night and day, whenever possible, for 4 weeks. Group 2 - **kinesiology tape**: Tape with a width of 5 cm and a thickness of 0.5 mm was used. Kinesio Tex I Strip was measured from elbow to fingertips and cut. It was folded approximately 2 blocks from the end and cut into 2 triangles on the fold. The 3rd and 4th fingers were slipped through holes and Kinesio Tex was applied on the dorsum of the hand with no tension. The position of elbow extension, wrist extension, and radial deviation was provided, and Kinesio Tex was applied from hand to medial epicondyle with 15% to 25% tension and ended at medial epicondyle with no tension. The second Kinesio Tex I Strip was measured for wrist size and cut. It was applied to the carpal tunnel region with 25% to 35% tension. This technique has been described by Kase and colleagues (Kase 1998). Applied tension to kinesiology tape were performed according to the visible pores on the kinesiology tape. Participants were taped by a doctor certified to apply kinesiology tape. Kinesiology tape was applied at the beginning of the week, to stay on for 5 days, with a 2-day rest, a total of 4 times. Group 3 - **sham kinesiology tape**: Tape with a width of 5 cm and a thickness of 0.5 mm was used. Kinesio Tex I Strip was applied without having the proper position and with no tension (in a manner inconsistent with the technique described in Group 1). Kinesiology tape was applied at the beginning of the week, to stay on for 5 days, with a 2-day rest, a total of 4 times. **All groups**: All participants received a home exercise programme during the 4 weeks, consisting of tendon-gliding exercises. To follow up and to improve compliance, each participant was asked to document in a supplied diary what they did, i.e. how many times they did each exercise in a day. The diaries were checked every visit.
Outcomes	Outcomes were assessed at 4 weeks 1. BCTQ Symptom Severity Scale (1 to 5 higher is worse) 2. BCTQ Functional Status Scale (1 to 5 higher is worse) 3. BCTQ Total score (1 to 5 higher is worse) 4. Pain level using a VAS (0 = no pain to 10 = worst pain possible) 5. Neuropathic pain using the DN4 Questionnaire to measure pain characteristics and sensory symptoms (0 to 10; ≥ 4 considered as neuropathic pain; 10 questions, 1 is given if the answer is “yes”, and a score of 0 is given if it is “no”) 6. Grip strength (mean of 3 consecutive tests) using a Riester Dynatest hand dynamometer; sitting with their shoulder abducted and neutrally rotated, elbow flexed at 90°, and forearm and wrist in neutral position
Funding	Not reported
COI	Not reported
Notes	We assumed by reading the paper that the follow-up data collection occurred at 4 weeks, but this was not explicitly stated.

Geler Kulcu 2016 *(Continued)*

VAS – data analysis implied that this was a Numerical Rating Scale, not a VAS.

Results from BCTQ not reported on a 1 to 5 scale. We assumed that investigators reported the total sum and divided the symptom score by 11 and the functional score by 8 (as per instructions of the scale).

The number of participants and hands reported in the main text and Figure 1 were not the same. We used data from Figure 1 as these data appeared to be correct.

Adherence to exercise was monitored by documenting what was done in a diary.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly assigned to one of the three groups using a secure system of opaque closed envelopes numbered 1–3. Wrists of the patients with bilateral CTS were allocated to the same group according to the envelope number that the patient chose. The first group received KT [kinesiology tape], the second group received sham KT, and the third group received an OD [orthotic device], performed by a researcher not involved in the study." Comment: The random sequence was probably adequately generated, as it appeared the participants randomly selected the envelope containing the randomisation allocation.
Allocation concealment (selection bias)	Low risk	Quote: "Patients were randomly assigned to one of the three groups using a secure system of opaque closed envelopes numbered 1–3. Wrists of the patients with bilateral CTS were allocated to the same group according to the envelope number that the patient chose. The first group received KT, the second group received sham KT, and the third group received an OD, performed by a researcher not involved in the study." Comment: The allocation sequence appeared to have been adequately concealed prior to assignment of interventions.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The investigator applying the treatments was different from the investigator evaluating the outcome measures; the latter was blind to which series of treatments (experimental KT, placebo KT, or OD) each patient was about to receive or had just received. The patients in Group 1 and Group 2 were blind to the treatments." Comment: The participants in Groups 1 and 2 were blinded to whether they were receiving the experimental or sham intervention. However, the participants in Group 3 were not blinded. Furthermore, due to the nature of the treatments, those providing treatment were unlikely to be blinded to the intervention groups.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The investigator applying the treatments was different from the investigator evaluating the outcome measures; the latter was blind to which series of treatments (experimental KT, placebo KT, or OD) each patient was about to receive or had just received." Comment: The outcome assessors were likely blinded to the treatment group. However, since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: The number of dropouts at 4-week follow-up: 1) kinesiology tape group: 2/15 (13%) 2) placebo kinesiology tape group: 2/15 (13%)

Geler Kulcu 2016 *(Continued)*

		3) orthotic device group 1/15 (7%) Dropouts and protocol violators are clearly documented in the flow diagram and were not included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: All outcomes specified in the methods were reported, but no study protocol was available, therefore the risk was unclear.
Other bias	Unclear risk	Quote: "Patients with bilateral symptoms were asked to complete two questionnaires, one for each hand separately." Comment: The unit of analysis was hands (with some participants contributing 2 hands to the analysis). Although unlikely, it was unclear whether a unit of analysis error may have occurred in the data analysis.

Hall 2013

Study characteristics	
Methods	Study design: randomised controlled 2-arm unblinded trial Setting: hospital clinic, Australia
Participants	**Details of sampling frame** Total n eligible = 116 Total n excluded pre-randomisation = unclear (58 participants were excluded because they did not meet the selection criteria) Total n randomised = 62 participants (hands) Intervention group 1 (splint and education) n = 31 participants (hands) Intervention group 2 (control - no treatment) n = 31 participants (hands) Post-intervention follow-up: Total n available for follow-up = 54 participants (hands) Total n analysed = 54 participants (hands) Intervention group 1 (splint and education) n available for follow-up = 30 participants (hands) Intervention group 2 (control - no treatment) n available for follow-up = 24 participants (hands) **Gender distribution** Intervention group 1 (splint and education): 9 males; 21 females Intervention group 2 (control - no treatment): 5 males; 19 females **Mean ± SD age:** Intervention group 1 (splint and education): 53.8 ± 5.6 Intervention group 2 (control - no treatment): 54.9 ± 4.7 **Mean (range) duration of CTS symptoms:** Intervention group 1 (splint and education): 28.3 (26-132) months

Hall 2013 *(Continued)*

	Intervention group 2 (control - no treatment): 37.9 (28-132) months **Inclusion criteria** 1. Age 18 years or older 2. Paraesthesia in the median nerve distribution in the night or day 3. Clumsiness 4. Grasp weakness 5. Sleep disturbance 6. No medical intervention (e.g. no surgery or corticosteroid injection) 7. No conservative treatments (e.g. no wearing of hand splints) in the past 6 months 8. No pregnancy **Exclusion criteria:** Any medical, cognitive, perceptual, or language deficits that prevented the comprehension of instructions or attendance at appointments **CTS diagnostic criteria (case definition):** Not reported **CTS severity:** Not reported **Protocol violators:** Intervention protocol violators were not included in the analysis.
Interventions	Group 1 -**splint and education:** 8-week treatment programme involving a full-time wrist splint and education sessions conducted by an occupational therapist. The programme included prescription and fitting of a wrist-support splint and structured education sessions with a focus on self-management. Over the 8-week period, each participant received 2 treatment sessions in the 1st week and between week 2-4 and a 20 min phone call at week 7. The wrist splint positioned the wrist in a neutral wrist position and allowed full finger and thumb motion. One of 4 choices of splint were provided: Otto Bock Manu Basic; Roylan Enlarged Thumb Hole D-Ring Wrist Brace; Otto Bock Manu Comfort; or custom-made thermoplastic wrist splint. Education included pathology of CTS, risk identification, and goal setting designed to teach self-management of CTS symptoms e.g. avoidance of tasks that aggravate symptoms. The night-time compliance rate for wearing the splint averaged 89%, but compliance dropped to 81% during the daytime. Group 2 - **control:** participants were assessed and observed but received no intervention during the 8-week study period.
Outcomes	The outcomes were measured at baseline and at 8 weeks. 1. BCTQ symptoms severity score (1 to 5 higher is worse) 2. BCTQ functional status score (1 to 5 higher is worse) 3. BCTQ total score 4. Pain VAS (0 = no pain to 10 = worst pain) 5. Grip strength using a Jamar dynamometer. The American Society of Hand Therapists Clinical Assessment Recommendations were used for testing procedures and calibration. 6. Finger dexterity using Purdue Pegboard Test (higher time indicates impaired dexterity) 7. Sensibility using Semmes Weinstein monofilaments score using the American Society of Hand Therapists (ASHT) Clinical Assessment Recommendations (lower value indicates better sensation) 8. Provocative CTS test: Phalen's test (positive/negative) 9. Perceptions of treatment effect in 9-item questionnaire (each item 0 = strongly disagree 10 = strongly agree) 10. Desire to seek surgery

Hall 2013 *(Continued)*

Funding	Not reported
COI	Not reported
Notes	We decided to include this study in splint versus no active treatment (education about the condition was considered as non-disease modifying side intervention as in the other analyses where the participants received information about the condition). We did not include the data regarding referral to surgery because of partial reporting: Study reported that 19/30 participants (63%) had decided not to pursue surgical intervention after the CTS conservative treatment programme (which implies that 11/30 participants had still opted for surgery); however, the outcome was not reported for the control group. The night-time compliance rate for wearing the splint averaged 89%, but compliance dropped to 81% during the daytime.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants who were invited and agreed to participate in the study were randomly assigned to the intervention or control group using a blocking strategy, implemented by the first author, to recruit participants to each study arm at equal rates." Comment: It is likely that sequence generation was adequate.
Allocation concealment (selection bias)	Unclear risk	Comment: It is not clear from the publication whether the allocation sequence was adequately concealed until the interventions were assigned.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The two treating occupational therapists, who were not blinded to group allocation, performed all data collection and provided interventions according to the study's assessment and treatment procedure manual." Comment: Due to the nature of the interventions, it is unlikely that participants were blinded. The treating therapists were not blinded to the interventions.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The two treating occupational therapists, who were not blinded to group allocation, performed all data collection and provided interventions according to the study's assessment and treatment procedure manual." Comment: However, since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	High risk	Quote: "31 were assigned to each group (treatment and control group). Eight participants withdrew, were excluded, or did not complete the study after group allocation (1 from the treatment group and 7 from the control group). The reasons for non-compliance included vocational requirements that prohibited wearing of splints during work hours and habitual participation in activities such as swimming or cooking that precluded wearing a splint. Discomfort and perceived negative cosmetic effects were also reported as reasons not to wear splint." Comment: All participants were accounted for and reasons for dropouts and attrition were documented, but the loss was not balanced 1/31 (3%) versus 7/31 (23%).

Hall 2013 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Comment: All the outcomes specified in the methods reported, but no study protocol available, therefore the risk was unclear.
Other bias	Low risk	Quote: "Participants could have symptoms in one or both hands, but only one hand, with the worst symptoms, was chosen as the study hand". Comment: Only 1 hand for each participant was enrolled in the study, therefore a unit of analysis error was not observed. All outcomes were measured using appropriate reliable and valid methods.

Jaladat 2017

Study characteristics	
Methods	Study design: RCT Setting: Iran
Participants	**Details of sampling frame:** Total n eligible = not reported Total n excluded pre-randomisation = not reported Total n randomised = 24 Total n available for follow-up = 24 Total n analysed = 24 Intervention group 1 (splint + routine rehabilitation) n = 12 Intervention group 2 (routine rehabilitation) n = 12 **Gender distribution:** Intervention group 1 (splint + routine rehabilitation): 0 males, 12 females Intervention group 2 (routine rehabilitation): 0 males, 12 females **Mean ± SD age:** Intervention group 1 (splint + routine rehabilitation): 47.42 years (SD not reported) Intervention group 2 (routine rehabilitation): 45.76 years (SD not reported) **Mean ± SD duration of CTS symptoms:** Not reported **Inclusion criteria:** 1. Female 2. Diagnosed with CTS by the physiatrist 3. Mild or moderate CTS 4. Able to understand and follow instructions **Exclusion criteria:** 1. History of surgery 2. Systemic diseases

Jaladat 2017 *(Continued)*

3. Pregnancy
4. Wrist-fracture histories
5. Lack of cooperation
6. Lack of nerve-conduction velocity results

CTS diagnostic criteria (case definition):

1. Classification of NCV findings to a cluster of mild, moderate, and severe CTS

1.1. Median nerve SDL (mild > 3.7; moderate > 4.5; severe > 5.3)

1.2. Median nerve wrist SNCV (mild < 40; moderate < 35; severe < 30)

1.3. Median nerve DML (mild > 4.5; moderate > 5.5; severe > 6.5)

1.4. Median motor response amplitude compared to other hand (mild - ; moderate < 50%; severe -)

1.5. Median nerve compound latency (mild > 2.4; moderate > 2.8; severe > 3.2)

1.6. Median nerve compound amplitude compared to other hand (mild < 50%; moderate - ; severe -)

CTS severity:

Mild-to-moderate

Interventions	Group 1 - **splint + routine rehabilitation**: treatment for 6 weeks. Splint: thermoplastic customised limited dynamic wrist splint (with a range of motion between 15° flexion & 15° extension), which they had to wear for 6 to 8 hours a day Group 2 - **routine rehabilitation**: treatment for 6 weeks (including activity/ergonomic modifications, nerve and tendon gliding exercises, massage, carpal bones and nerve mobilisations, stretches of upper extremity and flexor retinaculum)
Outcomes	Outcomes evaluated before treatment and 6 weeks after treatment 1. BCTQ symptom severity score (1 to 5 higher is worse) 2. BCTQ functional status score (1 to 5 higher is worse) 3. Dexterity test of a Purdue pegboard 4. Grip strength (kg) 5. Pinch strength (kg) 6. SDL (ms) 7. SNCV (m/s)
Funding	Not reported
COI	Authors reported no conflict of interest.
Notes	Results from BCTQ not reported on a scale of 1 to 5. We assumed that the total sum was reported and investigators divided the symptom score by 11 and the functional score by 8 (as per instructions of the scale).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "This interventional study was designed as a randomized controlled trial". "The patients were randomly divided into control and treatment groups". Comment: No further information provided about sequence generation provided

Jaladat 2017 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Quote: "The study was planned as a prospective, randomized, single-blind study." Comment: No further information provided about allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: No information about blinding provided, but splinting and routine rehabilitation treatment methods are obviously different from each other, therefore unlikely that the participants were blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: No information about blinding provided, but splinting and routine rehabilitation treatment methods are obviously different from each other, therefore unlikely that blinding was possible
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: No loss to follow-up reported
Selective reporting (reporting bias)	Low risk	Comment: All outcomes defined in the registration (IRCT2015061522753N1) and methods, were reported at 6 weeks.
Other bias	Low risk	Comment: In both groups, the participants could have rehabilitation including activity/ergonomic modifications, nerve and tendon gliding exercises, massage, carpal bones and nerve mobilisations, and stretches of the upper extremity and flexor retinaculum. The authors did not measure the use of co-interventions but no reason to assume that they would differ

Kocaoglu 2017

Study characteristics	
Methods	Study design: parallel-group, 3-arm RCT Setting: Turkey
Participants	**Details of sampling frame:** Total n eligible = not reported Total n excluded pre-randomisation = not reported Total n randomised = 60 Total n available for follow-up = not reported Total n analysed = not reported Intervention group 1 (splint) n = 20 Intervention group 2 (kinesiology tape) n = 20 Intervention group 3 (Steroid/local anaesthetic injection) n = 20 **Gender distribution:** Total: 2 males, 58 females Intervention group 1 (splint): not reported Intervention group 2 (kinesiology tape): not reported

Kocaoglu 2017 *(Continued)*

	Intervention group 3 (Steroid/local anaesthetic injection): not reported **Mean ± SD age:** Total: 48.2 ± 8.9 years Intervention group 3 (splint): not reported Intervention group 1 (kinesiology tape): not reported Intervention group 2 (Steroid/local anaesthetic injection): not reported **Mean ± SD duration of CTS symptoms:** Total: disease-duration, 2.8 + 3.5 months Intervention group 3 (splint): not reported Intervention group 1 (kinesiology tape): not reported Intervention group 2 (Steroid/local anaesthetic injection): not reported **Inclusion criteria:** 1. People with CTS **Exclusion criteria:** Not reported **CTS diagnostic criteria (case definition):** Not reported **CTS severity:** Not reported
Interventions	Group 1 - **splinting** for 3 weeks Group 2 - **kinesiology taping:** performed 3 times at 4-day intervals Group 3 - **a steroid/local anaesthetic injection** to carpal tunnel
Outcomes	The clinical and electrophysiologic studies were performed at baseline and at the 3rd week 1. BCTQ symptom severity score (1 to 5; higher is worse) 2. BCTQ functional ability score (1 to 5; higher is worse) 3. Pain VAS (0 to 100; higher indicates worse) 4. Motor latency (ms; higher is worse) 5. Sensory latency (ms; higher is worse) 6. Motor amplitude (mA; higher is better) 7. Sensory amplitude (mA; higher is better)
Funding	Not reported
COI	Not reported
Notes	Number of participants randomised in each group was not reported, but we assumed that the numbers were equal. Study reported as a congress abstract, not much information available

Kocaoglu 2017 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The patients were randomized into three groups receiving either KT performed three-times by intervals of 4-day (Group 1); a single S/LA injection to carpal-tunnel (Group 2); or splinting alone for three-weeks (Group 3)." Comment: Random sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Quote: "The patients were randomized into three groups receiving either KT performed three-times by intervals of 4-day (Group 1); a single S/LA injection to carpal-tunnel (Group 2); or splinting alone for three-weeks (Group 3)." Comment: Allocation concealment not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: The authors did not report any attempt at blinding. Due to the nature of the interventions, it is unlikely that participants were blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: Since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	Unclear risk	Comment: loss to follow-up not described
Selective reporting (reporting bias)	Unclear risk	Comment: All the outcomes specified in the methods reported, but no study protocol available, therefore the risk was unclear.
Other bias	Unclear risk	Comment: No apparent other sources of bias

Madjdinasab 2008

Study characteristics	
Methods	Study design: RCT Setting: Iran
Participants	**Details of sampling frame:** Total n eligible = not reported Total n excluded pre-randomisation = not reported Total n randomised = 48 participants Intervention group 1 (splint) n = 24 participants Intervention group 2 (oral steroid) n = 24 participants **Gender distribution:** Intervention group 1 (splint): 2 males, 22 females Intervention group 2 (oral steroid): 2 males, 22 females

Madjdinasab 2008 *(Continued)*

	Mean ± SD age: Intervention group 1 (splint): 43 years Intervention group 2 (oral steroid): 40 years Total mean: 42.19 (range 21 to 65 years) **Mean ± SD duration of CTS symptoms:** Not reported **Inclusion criteria:** 1. Clinical diagnosis of CTS for at least 1 month 2. Electrophysiological evidence of median neuropathy (defined as having 2 or more of the following: 1. Median nerve DML recording at abductor pollicis brevis and wrist stimulating greater than 4.4 ms; 2. Median nerve antidromic sensory peak latency recording at digit II greater than 3.5 ms; 3. Difference between antidromic median sensory latency and ulnar sensory latency at digit IV greater than 0.5 ms; 4. Antidromic latency difference more than 0.5 ms between median nerve at digit II and ulnar nerve at digit V; 5. The same distance of measurement). **Exclusion criteria:** 1. Diabetes mellitus, trauma to wrist and deformity 2. Evidence of generalised neuropathy or radiculopathy on electrodiagnostic study 3. Advanced CTS, having wasting, marked weakness with marked axonal loss on a NCS, or nonstimulatable nerves 4. History of peptic ulcer 5. Previous treatment for CTS using medical or surgical therapy 6. Pregnant women with CTS 7. Systemic disorders like rheumatoid arthritis, hypothyroidism, amyloidosis, etc. **CTS diagnostic criteria (case definition):** Electrophysiological criteria were used for diagnosis of CTS. **CTS severity:** Not reported
Interventions	Group 1 - **commercially available splint**: worn at night and for as long as possible during the day for 6 weeks (wrist splinting in neutral position) Group 2 - **oral steroid:** Prednisolone 20 mg/day for 2 weeks **Both groups** were given advice to avoid extreme wrist flexion/extension, excessive hand movement and hand rest. The participants were also asked not to use additional medicines or other methods of treatment during the study period.
Outcomes	Outcomes assessed at baseline and at the end of 6 weeks treatment 1. Median and ulnar nerve SDL (ms) 2. Median and ulnar nerve DML (ms) 3. Median and ulnar SNCV (m/s) 4. Median and ulnar MNCV (m/s)
Funding	Not reported
COI	Not reported

Madjdinasab 2008 *(Continued)*

Notes	No self-reported outcomes (e.g. symptoms, pain) or function outcomes were reported as being measured in this study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "They were randomly divided into two groups. Splint groups (N = 24) used splint for six weeks; and steroid group (N = 24) used oral Prednisolone 20 mg/day for two weeks." Comment: No information reported on how the randomisation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Quote: "They were randomly divided into two groups. Splint groups (N = 24) used splint for six weeks; and steroid group (N = 24) used oral Prednisolone 20 mg/day for two weeks." Comment: No information reported on how adequately the randomisation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "This double blind study was carried out in 48 idiopathic CTS patients". Comment: The authors reported that this was a double-blind study, but did not indicate who specifically was blinded (participants, personnel delivering the treatment, or outcome assessors). Due to the nature of the interventions (splint versus oral steroid), it is likely that participants were aware of their allocated treatment.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "This double blind study was carried out in 48 idiopathic CTS patients". Comment: The authors reported that this was a double-blind study, but did not indicate who specifically was blinded (participants, personnel delivering the treatment, or outcome assessors). Due to the nature of the interventions (splint versus oral steroid), it is likely that participants were aware of their allocated treatment.
Incomplete outcome data (attrition bias) 3 months or less	Unclear risk	Quote: "In splint group three patients and in steroid group two patients did not complete the study and were eliminated." Comment: 21/24 of the splint group and 22/24 of the prednisolone group completed assessments. The reasons for participants not completing the study were not reported, so it is not possible to determine whether the dropouts could have had an impact on the results.
Selective reporting (reporting bias)	Unclear risk	Comment: All outcomes reported in the Methods section of the publication were reported in the Results section of the publication. However, the only reported outcomes were electrophysiologic measures. Most other CTS RCTs also measured symptoms and function and without access to a protocol for this study, we could not determine whether those clinical outcomes were measured but not reported in the publication.
Other bias	Low risk	Comment: No other sources of bias identified

Manente 2001

Study characteristics

Methods	Study design: RCT Setting: Italy

Manente 2001 *(Continued)*

Participants	**Details of sampling frame:** Total n eligible = 151 screened Total n excluded pre-randomisation = not reported Total n randomised = 83 participants (83 wrists) Intervention group 1 (splint) n = 41 participants (41 wrists) Intervention group 2 (no treatment) n = 42 participants (42 wrists) Post-intervention follow-up: Total n available for follow-up = 80 participants (80 wrists) Total n analysed = 80 participants Intervention group 1 (splint) n = 40 participants (40 wrists) Intervention group 2 (no treatment) n = 40 participants (40 wrists) **Gender distribution:** Intervention group 1 (splint): 4 males, 36 females Intervention group 2 (no treatment): 7 males, 33 females **Mean ± SD age:** Intervention group 1 (splint): 46.10 ± 12.94 years Intervention group 2 (no treatment): 50.0 ± 12.65 years **Mean ± SD duration of CTS symptoms:** Not reported **Inclusion criteria:** 1. CTS symptoms (pain, numbness, paraesthesiae in median nerve distribution) exclusively or predominantly in one wrist 2. CTS signs (hypoaesthesia in median nerve distribution, thenar atrophy, positive Phalen's test) exclusively or predominantly in one wrist 3. At least one abnormal CTS electrodiagnostic study **Exclusion criteria:** 1. Previous CTS surgery 2. Rheumatoid arthritis 3. Systemic disease 4. Pregnancy 5. Clinical and electrophysiological signs of polyneuropathy **CTS diagnostic criteria (case definition):** On the basis of the electrophysiological results, hands were classified according to the following neurophysiological classification: 1. extreme CTS, absence of median motor and sensory response 2. severe CTS, absence of median sensory response and prolonged DML 3. moderate CTS, slowed digit II–wrist SNCV and abnormal DML 4. mild CTS, slowed median digit II–wrist SNCV and normal DML 5. minimal CTS, normal digit II–wrist SNCV and DML, but abnormal segmental or comparison tests

Manente 2001 *(Continued)*

	6. and negative, all tests normal
Interventions	Group 1 - **splint**: worn at night for 4 weeks (hand brace, called Manu) Group 2 - **control (no treatment)**: participants were asked to wait for an observational period of 4 weeks. **All participants** were required to agree not to receive other treatments, or change work duties or medications during the study, or otherwise report it.
Outcomes	Outcome assessed at 2 weeks and at the end of 4 weeks of treatment 1. BCTQ symptom severity score (1 to 5; higher is worse) 2. BCTQ functional status score (1 to 5; higher is worse) 3. Global impression of change (participant-rated questionnaire rated in 4 categories: moderate or much improvement, minimal improvement, no change, worsening) (at 4 weeks only) 4. Median DML (ms) (at 4 weeks only) 5. Median SNCV (m/s) (at 4 weeks only) 6. SNAP amplitude (uV) (at 4 weeks only) 7. Changes of electrophysiological class of severity (4 weeks only) 8. Compliance and tolerability 9. Adverse effects
Funding	This study was supported by a grant from the Italian Ministry for Scientific and Technological Research.
COI	First author is the owner of the patent for the brace, which was pending at the time of publication.
Notes	Compliance and tolerability was assessed by a questionnaire asking how many nights in 4 weeks the participant wore the hand brace: all 28 nights; most (at least 21) nights; half (about 14) of the nights; and some (less than 7) nights, and whether there were adverse effects. Of the 40 participants in the treated group, 38 wore the hand brace for all or most of the nights.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Subjects were randomized into two groups by having them select sealed envelopes containing a group assignment". Comment: Insufficient information provided to determine whether an adequate method was used to generate random sequence
Allocation concealment (selection bias)	Unclear risk	Quote: "Subjects were randomized into two groups by having them select sealed envelopes containing a group assignment". Comment: not specified whether envelopes were opaque or sequentially numbered and distributed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Participants, personnel, and outcome assessors were not blinded to treatment allocation (confirmed by study authors via personal communication). Assessment of symptoms, functional status, and global impression of change may be biased.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: However, since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.

Manente 2001 *(Continued)*

Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: Only 1 participant in the treatment group was lost to follow-up and 2 participants in the control group were excluded after randomisation because they underwent surgery. This is unlikely to have introduced substantial bias in the comparison of outcomes for each group.
Selective reporting (reporting bias)	Low risk	Comment: All outcomes stated in the methods section of the publication were reported in the results.
Other bias	High risk	Comment: First author is the owner of the patent for the brace, which was pending at the time of publication.

Mishra 2006

Study characteristics	
Methods	Study design: RCT Setting: neurology outpatient department of a tertiary care centre, India
Participants	**Details of sampling frame:** Total n assessed for eligibility = 66 participants (117 hands) Total n excluded pre-randomisation = 26 participants Total n randomised = 40 participants (71 hands) Total n available for follow-up = 40 participants (71 hands) Total n analysed = 71 wrists Intervention group 1 (splint) n = 20 participants (36 wrists) Intervention group 2 (oral steroid) n = 20 participants (35 wrists) **Gender distribution:** Intervention group 1 (splint): 3 males, 17 females Intervention group 2 (oral steroid): 4 males, 16 females **Mean ± SD (range) age:** Intervention group 1 (splint): 42.91 ± 9.39 (range 23 to 60) years Control group 2 (oral steroid): 41.57 ± 9.26 (range 28 to 60) years **Mean ± SD duration of CTS symptoms:** Intervention group 1 (splint): 6.40 ± 7.09 months Control group 2 (oral steroid): 6.31 ± 7.50 months **Inclusion criteria:** Symptoms suggestive of CTS of at least 1-month duration and electrophysiological evidence of median neuropathy at wrist **Exclusion criteria:** 1. Diabetes mellitus, trauma to wrist and deformity

Mishra 2006 *(Continued)*

2. Evidence of generalised neuropathy or radiculopathy on electrodiagnostic study
3. Advanced CTS having wasting, marked weakness with marked axonal loss on NCS or nonstimulatable nerves
4. History of peptic ulcer
5. Previous treatment for CTS using medical or surgical therapy
6. Pregnancy
7. Systemic disorders like rheumatoid arthritis, hypothyroidism, amyloidosis, etc.

CTS diagnostic criteria (case definition):

The clinical criteria laid down by the American Academy of Neurology were used for diagnosis of CTS. The electrophysiological criteria used for the diagnosis of CTS included the presence of 2 or more of the following:

1. Median nerve DML recording at abductor pollicis brevis and stimulating at wrist greater than 4.4 ms
2. Median nerve antidromic sensory peak latency recording at digit II greater than 3.5 ms
3. Difference between antidromic median sensory latency and ulnar sensory latency at digit IV greater than 0.5 ms
4. Antidromic latency difference of > 0.5 ms between median nerve at digit II and ulnar nerve at digit V using the same distance of measurement

CTS severity:

Not reported

Interventions	Group 1 - **commercially available carpal tunnel splint**: worn in the neutral position at night and as much as possible during the daytime for 4 weeks. In the case of bilateral symptoms, both hands were treated. Participants were also told not use additional medicines or other methods of treatment during the study period. Group 2 - **oral steroid**: prednisolone 20 mg/day was taken for 2 weeks followed by 10 mg/day for another 2 weeks. Advice to avoid extremes of wrist flexion or extension, excessive hand movement and hand rest was common to **both groups**.
Outcomes	Outcomes assessed before treatment and at the end of 4 weeks of treatment and at 8 weeks post-treatment: 1. BCTQ symptom severity score (1 to 5; higher is worse) 2. BCTQ functional status score (1 to 5; higher is worse) 3. Median nerve DML (ms) 4. Median nerve MCV (m/s) 5. Median nerve SDL (ms) 6. Median nerve SNCV (m/s) 7. Adverse effects: measured as the number of participants experiencing adverse effects (e.g. discomfort and swelling of the hands and wrist)
Funding	Not reported
COI	Not reported
Notes	Compliance was reported as excellent in steroid group, while 3 participants were not using splint regularly as prescribed (only 5 to 6 days per week instead of most of the time daily as advised) also taking NSAIDs like nimesulide and diclofenac.
Risk of bias	

Mishra 2006 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was done using the table of random numbers." Comment: The randomisation sequence was probably adequately generated.
Allocation concealment (selection bias)	Unclear risk	Quote: "All patients were randomly allocated to one of the following two groups: 1. Splinting in neutral position. 2. Oral steroid. Randomization was done using the table of random numbers." Comment: Not enough information to determine whether the treatment allocation was adequately concealed until interventions were assigned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "A prospective randomised open-label clinical and electrophysiological study of efficacy of splinting and oral steroids for the treatment of CTS was done." Comment: Participants were probably aware of which intervention they received.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: Since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: No withdrawals, dropouts or losses to follow-up were reported, and the authors indicated in the results tables that data was based on all 71 randomised wrists.
Selective reporting (reporting bias)	Low risk	Comment: All of the study's outcomes (prespecified in the Methods section of the study report) were reported in the prespecified way.
Other bias	Low risk	Comment: No other sources of bias identified

Oncu 2014

Study characteristics	
Methods	Study design: RCT, blind assessor Setting: physical therapy outpatient clinic, Turkey
Participants	**Details of sampling frame:** Total n eligible = not reported Total n excluded pre-randomisation = not reported Total n randomised = 40 participants (60 wrists) Total n available for follow-up = 40 participants (60 wrists) Total n analysed = 40 participants (60 wrists) Intervention group 1 (splint + exercise) n = 15 wrists Intervention group 2 (kinesiology tape + exercise) n = 15 wrists Intervention group 3 (kinesiology tape + splint + exercise) n = 15 wrists

Oncu 2014 *(Continued)*

Intervention group 4 (exercise) n = 15 wrists

Gender distribution:

Intervention group 1 (splint + exercise): not reported

Intervention group 2 (kinesiology tape + exercise): not reported

Intervention group 3 (kinesiology tape + splint + exercise): not reported

Intervention group 4 (exercise): not reported

Total: 40 females, 0 males

Mean ± SD (range) age:

Intervention group 1 (splint + exercise): not reported

Intervention group 2 (kinesiology tape + exercise): not reported

Intervention group 3 (kinesiology tape + splint + exercise): not reported

Intervention group 4 (exercise): not reported

Total: 48.97+10.66

Mean ± SD (range) duration of CTS symptoms:

Intervention group 1 (splint + exercise): not reported

Intervention group 2 (kinesiology tape + exercise): not reported

Intervention group 3 (kinesio tape + splint + exercise): not reported

Intervention group 4 (exercise): not reported

Inclusion criteria:

1. Pain or numbness extending to the palmar side of the hand
2. At least 1 of the following positive: Tinel's sign, Phalen's test or carpal compression tests
3. Symptoms present at least for 3 months
4. Mild or moderate CTS diagnosed by ENMG
5. Being literate

Exclusion criteria:

1. Severe CTS
2. Having thenar atrophy
3. Steroid injection, medical or physical therapy for CTS
4. Secondary CTS (thyroid functional disorders, diabetes mellitus, pregnancy, connective tissue disorders)
5. Diseases with neck and arm pain (cervical disc herniation, rotator cuff syndrome, epicondylitis, de Quervain tenosynovitis, trigger finger, Dupuytren contracture, fracture in the wrist, more proximal upper extremity entrapment neuropathies, polyneuropathy, peripheral nerve injury, fibromyalgia syndrome) which may affect the symptoms

CTS diagnostic criteria (case definition):

1. Pain or numbness extending to the palmar side of the hand
2. At least 1 positive test (Tinel, Phalen, or carpal compression tests)
3. Symptoms present at least for 3 months
4. Mild or moderate CTS diagnosed by ENMG

CTS severity:

Oncu 2014 *(Continued)*

	Mild-to-moderate
Interventions	Group 1 -**splint and exercise** (tendon and nerve gliding exercises for 25 days): Participants received a splint in a neutral position with a volar support which allowed wrist pronation and supination while extension and deviation were restricted. Participants were recommended to use the splint at night for 25 days. Group 2 -**kinesiology taping and exercise** (tendon and nerve gliding exercises for 25 days): kinesiology taping was performed using neural technique and ligament technique/space correction techniques. which are recommended for CTS. Group 3 - **kinesiology taping** (see above) **and splint** (see above) **and exercise** (tendon and nerve gliding exercises for 25 days) Group 4 - **exercise only:** (tendon and nerve gliding exercises for 25 days)
Outcomes	Outcomes assessed at 25 days post-randomisation, and 2 and 3 months follow-up 1. BCTQ symptom severity score (scores between 11 and 55; higher scores are compatible with increased symptom severity) 2. BCTQ functional status score (scores between 8 and 40; higher values corresponds to impaired hand functionality) 3. Grip strength using Jamar hand dynamometer (measured in kg) 4. Lateral pinch strength using Jamar hand dynamometer (measured in kg) 5. Tip pinch strength using Jamar hand dynamometer (measured in kg) 6. Hand skills measured using the Moberg Pickup test 7. SNCV 8. MNCV
Funding	The authors declared that this study has received no financial support.
COI	No conflict of interest was declared by the authors.
Notes	Article in Turkish, translation used BCTQ results reported as mean from 1 to 5 (higher is worse) in the article, table 1 and 2 Results for BCTQ functional status score provided for 3 months only (not for 25 days and 2 months) The authors reported that 10 of 40 participants had bilateral CTS, however the total number of wrists in the study were 60 (not 50). We used 40 as the number of participants (60 wrists) in the analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote from translation: "Four different treatment alternatives were created via computer by a statistical expert and the same person enumerated from high to low in an order and put them into envelopes. 40 patients were assigned to 4 groups according to the sequential (ranking) randomization method. The person who performs the therapy opened the envelope and carried out the treatment method from the envelope regarding the number of the patient."
Allocation concealment (selection bias)	Low risk	Quote from translation: "Four different treatment alternatives were created via computer by a statistical expert and the same person enumerated from high to low in an order and put them into envelopes. 40 patients were assigned to 4 groups according to the sequential (ranking) randomization method. The person who performs the therapy opened the envelope and car-

Oncu 2014 *(Continued)*

		ried out the treatment method from the envelope regarding the number of the patient."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Study was single (observer)-blind. Given the nature of the assigned interventions, participants were not blind.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote from translation: "One and same blind observer filled the assessment forms of all patients included in the study before, at 25th day (end of the study) and 2 and 3 months after the study. All patients were evaluated by EN-MG by the same and blind (for the treatment) observer before and 3 months after the study in the same ENGM laboratory." Comment: Since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: No dropouts reported, and data reported as being based on all wrists that were randomised (n = 60)
Incomplete outcome data (attrition bias) After 3 months	Low risk	Comment: No dropouts reported, and data reported as being based on all wrists that were randomised (n = 60)
Selective reporting (reporting bias)	Unclear risk	Comment: No protocol available, and outcome data not reported for all outcomes at all time points, but unclear if this was related to the nature of the findings
Other bias	High risk	Quote: "The same treatment method from a single envelope was implemented for both hands of cases having bilateral CTS (10 of 40 cases) not to influence the study results." Comment: There were 40 participants, with 60 wrists affected. Analysis was based on the number of wrists, and there was no attempt to adjust the analysis for the correlation between wrists.

Premoselli 2006

Study characteristics	
Methods	Study design: quasi-RCT Setting: outpatient clinic, Italy
Participants	**Details of sampling frame:** Total n eligible = not reported Total n excluded pre-randomisation = not reported Total n randomised = 50 participants (50 wrists) randomised Intervention group 1 (splint) n = 25 participants (wrists) Intervention group 2 (no treatment) n = 25 participants (wrists) Post-intervention follow-up at 3 months:

Premoselli 2006 *(Continued)*

	Total n available for follow-up = 49 participants (wrists) Total n analysed = 48 participants (wrists) Intervention group 1 (splint) n = 24 participants (wrists) Intervention group 2 (no treatment) n = 24 participants (wrists) Post-intervention follow-up at 6 months: Total n available for follow-up = 41 participants (wrists) Total n analysed = 34 participants (wrists) Intervention group 1 (splint) n = 18 participants (wrists) Intervention group 2 (no treatment) n = 16 participants (wrists) **Gender distribution:** Intervention group 1 (splint): 2 males, 23 females Intervention group 2 (no treatment): 3 males, 22 females **Mean ± SD age:** Intervention group: 53.1 ± 13.3 yrs Control group: 46.5 ± 13.8 yrs **Mean ± SD duration of CTS symptoms:** Not reported **Inclusion criteria:** 1. CMAP median nerve distal latency < 4.7 ms 2. Difference between median and ulnar SNAP latencies > 0.4 ms **Exclusion criteria:** 1. Diabetes 2. "Clear CTS" (i.e. not mild recent onset CTS, as measured using electromyographic measures) **CTS diagnostic criteria (case definition):** Electrodiagnostic evaluation **CTS severity:** Mild CTS
Interventions	Group 1 - **neutral custom-moulded thermoplastic resin wrist splints**: worn at night-time only, for a minimum of 6 hours per night, for 6 months Group 2 - **no intervention:** participants simply monitored
Outcomes	Outcomes assessed at baseline, at 3 months, and at the end of 6 months of treatment: 1. BCTQ questionnaire, symptom severity score (1 to 5; higher is worse) 2. BCTQ questionnaire, functional ability score (1 to 5; higher is worse) 3. SNAP latency (ms) 4. SNAP velocity (m/s) 5. SNAP amplitude (μV) 6. Motor action potential latency (ms)

Premoselli 2006 *(Continued)*

7. Motor action potential velocity (m/s)
8. Motor action potential amplitude (mV)
9. Semeiotic testing using the Williams and colleagues (Williams 1992) pressure-provocative test and the Phalen's test. The time lapse between the moment of stimulation and the first manifestation of symptoms was assessed for each kind of test.

Funding	Not reported
COI	Not reported
Notes	At the 6-month follow-up visit, 1/25 case group participants dropped out from the study because of surgical treatment, and 5/25 control group dropouts underwent surgical treatment; 2/25 case group participants dropped out because they failed to comply adequately with wearing the splint.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "The randomisation protocol was based on the last visit booking number (even or odd)." Comment: The trial authors used a non-random component in the sequence generation process.
Allocation concealment (selection bias)	High risk	Quote: "The randomisation protocol was based on the last visit booking number (even or odd)." Comment: The trials authors did not adequately conceal the treatment allocation until interventions were assigned.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Due to the nature of the interventions, it is likely that participants were aware of which treatment they received (night-time splint or no intervention).
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The examiner was blinded to treatment status (control or treatment)." Comment: Since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	Unclear risk	Quote: "Fifty patients (50 hands) were enrolled, of which 36 completed the study at 6 months." Quote: "At the three-month follow-up visit, 24/25 case patients and 24/25 control patients were evaluated." Quote: "At the six-month follow-up visit, 18 case group subjects and 16 control group subjects were evaluated." Comment: The numbers in these 3 quotes do not add up. In the abstract, it says that 36 participants were available at 6 months follow-up, but in the text, it says that 34 (18 + 16) participants were available at 6 months follow-up. Therefore, it is not clear how many participants were lost to follow-up and the reasons for these losses. Furthermore, 7 (3 versus 4) participants at long-term follow-up were excluded due to not adhering to the treatment, which may cause bias, but loss seems to be balanced between the groups.
Selective reporting (reporting bias)	Low risk	Comment: All outcomes stated in the methods section of the publication were reported as prespecified.

Premoselli 2006 *(Continued)*

Other bias	Low risk	Comment: No other sources of bias identified

Rioja Toro 2012

Study characteristics	
Methods	Study design: a prospective, blinded, randomised, placebo-controlled study Setting: Traumatology and Rehabilitation Service, Spain
Participants	**Details of sampling frame:** Total n eligible = not reported Total n excluded pre-randomisation = not reported Total n randomised = 49 (98 hands) Total n available for follow-up = unclear Total n analysed = 86 hands Intervention group 1 (splint & real laser) n = 22 hands Intervention group 2 (splint & placebo laser) n = 23 hands Intervention group 3 (real laser) n = 24 hands Intervention group 4 (placebo laser) n = 17 hands **Gender distribution:** Total: 3 males; 46 females Intervention group 1 (splint & real laser): not reported Intervention group 2 (splint & placebo laser): not reported Intervention group 3 (real laser): not reported Intervention group 4 (placebo laser): not reported **Mean ± SD (range) age:** Total: 49 ± 11.1 Intervention group 1 (splint & real laser): not reported Intervention group 2 (splint & placebo laser): not reported Intervention group 3 (real laser): not reported Intervention group 4 (placebo laser): not reported **Mean ± SD (range) duration of CTS symptoms:** Not reported **Inclusion criteria:** 1. Mild-to-moderate CTS **Exclusion criteria:**

Rioja Toro 2012 *(Continued)*

1. Inflammatory diseases (rheumatoid arthritis)
2. Traumatic causes (wrist fractures)
3. Neurological causes (radiculopathies, polyneuropathies),
4. Intracanal expansive processes (ganglions, tumours, osteophytes, etc.)
5. Joint deformities of the wrists and hands
6. Multiple sclerosis
7. Amyotrophic lateral sclerosis
8. Thoracic outlet syndrome
9. Polyneuropathies
10. Recent wrist fractures
11. Ulnar nerve entrapment in associated wrist or elbow

CTS diagnostic criteria (case definition):

1. The diagnostic criteria are those recommended by the American Academy of Emergency Medicine:

1.1. Sensory latency difference (degree of CTS: mild < 0.5 ms; moderate 0.5-0.8 ms; severe > 0.8 ms or not evoked)

1.2. Spontaneous activity at rest (degree of CTS: mild - not; moderate - not; severe - yes (sometimes))

1.3. Voluntary activity (degree of CTS: mild - normal; moderate - normal; severe - neurogenic pattern)

1.4. DML (degree of CTS: mild - normal; moderate - normal or slight increase; severe - augmented)

1.5. Motor potential synchronisation (degree of CTS: mild - yes; moderate - yes; severe - desynchronised or decreased in amplitude, or both)

1.6. Motor driving speed (degree of CTS: mild - normal; moderate - normal; severe - diminished)

CTS severity:

Mild-to-moderate CTS

Interventions	Group 1 -**splint during night & laser treatment** Group 2 - **splint during night & placebo** Group 3 - **laser treatment** Group 4 - **control (placebo laser)** For participants wearing splint: wrist orthosis with palmar metal strap was used (night-time), without encompassing the metacarpophalangeal joints and in a neutral wrist position (0° position). In all participants treated with real laser, a total energy dose of 945 J was used in an area of 4 x 4 cm^2 (59 J/cm^2) and of 5 J of total dose in the same area of 4 x 4 cm^2 (0.3 J/cm^2) in the treatments with placebo laser. The rhythm of the sessions has been 5 per week for 4 weeks. In all of them, a careful cleaning of the skin was carried out prior to each treatment session, to avoid losses due to reflection. **All participants** had either not started treatment with NSAIDs, or had stopped at least 1 month before. None were undergoing local treatments with iontophoresis, ultrasounds, etc., or they had abandoned it more than a month ago.
Outcomes	Outcomes evaluated before treatment and 1 and 3 months after treatment 1. Functional scale 2. BCTQ scale 3. Difference in the values of sensory latency times between the 4th-middle finger and the 4th-ulnar finger 4. DML

Rioja Toro 2012 *(Continued)*

Funding	Not reported
COI	The authors declared that they had no conflict of interest.
Notes	Article in Spanish, translation used The number of participants and hands reported in the main text and table 6 seems to be not the same - we used data from table 6, assuming that the table 6 reported hands.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The patients who passed the selection of units A and B, went to unit C (physiotherapy) where, randomly, one wrist was treated with Lv and the other with Lp (total 49 hands with Lv and 49 hands with Lp). Also, 27 patients were randomly indicated to use a wrist orthosis with palmar metal strap (night use), without encompassing the metacarpophalangeal joints and in a neutral wrist position (0°position); in 15 of them the orthosis was put on the most affected hand, and in 12 on both hands (total 39 hands with orthosis)." Comment: Not clear how the randomisation was done
Allocation concealment (selection bias)	Unclear risk	Comment: No information regarding the method of allocation was reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Blinding of real laser versus placebo laser probably possible, however, it is unlikely that blinding for orthosis was possible.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: Due to the nature of the interventions, it is likely that participants were aware of which treatment they were allocated to, therefore we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	Unclear risk	Comment: No flowchart and not completely clear if all participants were followed up or if the authors only reported data for those that participated in the follow-up visits.
Incomplete outcome data (attrition bias) After 3 months	Unclear risk	Comment: Numbers of participants not reported
Selective reporting (reporting bias)	Unclear risk	Comment: The outcomes were reported incompletely (only as P values from statistical analysis).
Other bias	Unclear risk	Comment: 49 participants had bilateral CTS (98 hands). The unit of analysis (hand or participant) was unclear, as the tables reported data for 86 participants.

Sanaee 2017

Study characteristics

Methods	Study design: 2-arm RCT

Sanaee 2017 *(Continued)*

	Setting: outpatient clinics of physical medicine and rehabilitation of Shiraz University of Medical Sciences
Participants	**Details of sampling frame:** Total n assessed for eligibility = 140 Total n excluded pre-randomisation = 22 Total n randomised = 118 Intervention group 1 (short-term splinting) n = 59 participants (94 hands) Intervention group 2 (long-term splinting) n = 59 participants (94 hands) Post-intervention follow-up: Total n available for follow-up = 94 participants (156 hands) Total n analysed = 94 participants (156 hands) Intervention group 1 (short-term splinting) n = 80 hands Intervention group 2 (long-term splinting) n = 76 hands **Gender distribution:** Intervention group 1 (short-term splinting): not reported Intervention group 2 (long-term splinting): not reported **Mean ± SD age:** Intervention group 1 (short-term splinting): 47.4 ± na Intervention group 2 (long-term splinting): 45 ± na **Mean ± SD duration of CTS symptoms (months):** Intervention group 1 (short-term splinting): 7.8 ± na Intervention group 2 (long-term splinting): 7.9 ± na **Inclusion criteria:** 1. CTS diagnosed by a physiatrist 2. At least one of the following criteria: a. thenar atrophy b. median nerve CMAP amplitude of 3.8 mV or less c. absent SNAPs of median nerve at wrist d. or needle electromyographic evidence of acute denervation of abductor pollicis brevis muscle e. and had rejected surgical management, despite it being strongly recommended to them **Exclusion criteria:** 1. History of previous surgery on the hand or wrist 2. Any mass, tumour, or deformity in the hand or wrist 3. Severe trauma to the wrist (such as a fracture) 4. Polyneuropathy 5. Cervical radiculopathy 6. Current pregnancy or lactation 7. Fibromyalgia, or 8. Arthritis

Sanaee 2017 *(Continued)*

	CTS diagnostic criteria (case definition): Not reported (included only severe as defined in the inclusion criteria) **CTS severity:** Severe CTS
Interventions	Group 1: NSAID (naproxen 500 mg 3 times a day) for 10 days, vitamin B_1 and B_6 tabs for 6 weeks, physiotherapy (paraffin bath with controlled temperature, ultrasound under water and grip exercise), and Dr.K.H. **splint** (a wrist splint keeping the wrist in 5° of dorsiflexion), for 6 weeks Group 2: the group received the same medical and physical therapy as the first group, **splint** 23 hours/day for the first 6 weeks, continuing use just at night till 6 months. **Both groups** also received recommendation for activity modification.
Outcomes	Outcomes were assessed at baseline and at 6 weeks and 6 months. 1. BCTQ symptom severity score (1 to 5; higher is worse) 2. BCTQ functional status score (1 to 5; higher is worse) 3. CMAP amplitude (higher is better) 4. CMAP latency (lower is better)
Funding	Not reported
COI	Not reported
Notes	Of all the 118 participants entering the study, 4 participants (3%) left the study going through the surgery. SD for outcomes were not provided in the article, but we calculated them from P value. The authors reported that 5 participants in the short-term group and 15 participants in the long-term group did not comply with the treatment (these participants were regarded as study dropouts).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "After filling in the informed consent, the subjects entered our study and randomly divided into two groups. We first randomized the patients with bilateral and then patients with unilateral severe CTS so that each group contains the same number of bilateral and unilateral involvement." Comment: Random sequence generation was not described.
Allocation concealment (selection bias)	Unclear risk	Comment: Allocation concealment was not described.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Blinding of participants not reported, but due to the nature of the interventions, it is likely that participants were aware of which treatment they were allocated to.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Both groups went under the evaluation of symptoms and function with CTSAQ (Boston questionnaire) and electrodiagnostical study by the same blind physiatrist at six weeks, and six months after the beginning of the study."

Sanaee 2017 *(Continued)*

		Comment: Since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: Follow-up data available for 80/94 (85%) in group 1 and 76/94 (81%) in group 2. The loss and reasons were comparable; differences were so small that they are unlikely to bias the results.
Incomplete outcome data (attrition bias) After 3 months	Low risk	Comment: Follow-up data available for 80/94 (85%) in group 1 and 76/94 (81%) in group 2. The loss and reasons were comparable; differences were so small that they are unlikely to bias the results.
Selective reporting (reporting bias)	Unclear risk	Comment: No protocol available to check. All outcomes described in the methods were reported. Adverse events not reported; unclear if measured
Other bias	Unclear risk	Comment: Clustering not controlled (hand was the subject). The number of participants with bilateral disease was balanced. Unclear if this could cause bias. Normal distribution not tested, T-test used; variances not given in the results

Schmid 2012

Study characteristics	
Methods	Study design: randomised, single-centre, assessor-blinded, controlled pilot study Setting: Princess Alexandra Hospital Australia (people awaiting electrodiagnostic testing)
Participants	**Details of sampling frame:** Total n assessed for eligibility = 111 Total n excluded pre-randomisation = 90 Total n randomised = 21 Total n available for follow-up = 21 Post-intervention follow-up: Total n analysed = 20 Intervention group 1 (splinting) n = 10 Intervention group 2 (exercise) n = 10 **Gender distribution:** Intervention group 1 (splinting): 7 males; 3 females Intervention group 2 (exercise): 5 males; 5 females **Mean ± SD age:** Group 1: 57.9 ± 16.3 Group 2: 49.9 ± 12.5 **Mean ± SD duration of symptoms (months):** Group 1: 62.8 ± 56.1 Group 2: 54.6 ± 47.6 **Inclusion criteria:** 1. Meeting clinical and electrodiagnostic criteria for mild or moderate CTS **Exclusion criteria:**

Schmid 2012 *(Continued)*

1. Severe electrodiagnostic findings
2. Electrodiagnostic findings were indicative of peripheral neuropathies other than CTS
3. Presence of inflammatory disease
4. History of previous surgery or trauma to the upper limb or neck
5. Any kind of treatment for CTS was received in the 3 months before testing
6. CTS was related to pregnancy or diabetes
7. Contraindication to magnetic resonance imaging examination

CTS diagnostic criteria (case definition):
Clinical findings and electrodiagnostic mild or moderate grade findings

CTS severity:

Mild or moderate CTS

Interventions	Group 1 - **splinting:** Participants received a prefabricated wrist splint (Access Health, Blackburn, Australia) that they wore at night for 1 week. All participants, irrespective of their treatment allocation, were encouraged to continue with their normal daily activities. Group 2 - **exercises:** 1-week home programme of nerve and tendon gliding exercises. The programme was instructed by a physiotherapist specialised in musculoskeletal management. For the tendon gliding exercises, the hand positions described by Wehbe and colleagues (Wehbe 1985) were adopted in 4 separate exercises. The nerve gliding exercises were based on recent biomechanical insights. Rather than progressively elongating the median, nerve exercises were selected which maximise nerve excursion while minimising an increase in nerve strain. The exercises were preceded by one warming-up exercise that included forward and backward rolling of the shoulder girdle. Ten repetitions of each exercise were performed per session. One session took approximately 2 min to complete. Participants were asked to complete 10 sessions per day. On the day of the 1-week follow-up assessment, no exercises were performed in order to evaluate the prolonged rather than immediate effects of exercise. Participants were instructed that exercises should not provoke any symptoms. If symptoms were provoked, it was recommended to continue the exercise regimen using a smaller range of motion. Each participant was contacted by phone after the 1st and 3rd day to ensure that the prescribed exercise regimen did not cause any discomfort. Exercise compliance was monitored with a diary.
Outcomes	Outcomes were collected after first 10-minute session of treatment and 1 week after recruitment. 1. BCTQ symptom severity score (1 to 5; higher is worse) 2. BCTQ functional status score (1 to 5; higher is worse) 3. Signal intensity change on MRI T2 weighted images on three levels (inlet, middle, outlet) and palmar bowing of transverse carpal ligament 4. Patient-specific functional scale (0 to 10; higher score indicates better function) 5. Pain on VAS (0 to 10; assumed 0 no pain, 10 worst) 6. Numbness on VAS (0 to 10; assumed 0 no numbness, 10 worst) 7. Adverse events
Funding	The study was funded through the Health Practitioner Research Scheme from Queensland Health, Australia and Project grant 511161 from the National Health and Medical Research Council (NHMRC) of Australia.
COI	All authors declared no conflict of interest.
Notes	Total BCTQ reported in the article, but results of Symptom Severity Scale and Functional Status Scale were sent to us by the author. Pain, numbness and BCTQ only collected/reported at baseline and 1 week (not after the 1st treatment). Direction of VAS not explicitly declared: “visual analogue scales (VAS) were completed for current level of pain and numbness (ranging from no pain/numbness to worst ever pain/numbness)”.

Schmid 2012 *(Continued)*

	All participants received the treatment as allocated and adhered to the prescribed exercise programme and splinting regimen.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients who met clinical and electrodiagnostic criteria for mild or moderate CTS (S-Table 1) were randomly allocated to receive either night splinting (n = 10) or nerve and tendon gliding exercises (n = 10; Fig. 1). Allocation was stratified for CTS severity based on electrodiagnostic test results." Comment: "The method of sequence generation not declared
Allocation concealment (selection bias)	Low risk	Quote: "Concealed random allocation was performed by an independent investigator using sealed envelopes."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Blinding of participants not reported, but due to the nature of the interventions, it is likely that participants were aware of which treatment they were allocated to.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "All MRI [magnetic resonance imaging] scans were coded and an investigator blinded to the group allocation took all measurements". Comment: Since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Quote: "21 patients were recruited from a list of patients awaiting electrodiagnostic testing at a neurology department of a public hospital. One patient discontinued the study after the first appointment due to time constraints."
Selective reporting (reporting bias)	Low risk	Comment: All outcomes which were planned in methods were reported. Considering the aims of this pilot study, it seems improbable that some outcomes were left unreported. Protocol could not be found in ICTRP or Clinicaltrials.gov.
Other bias	Low risk	Comment: No other sources of bias identified

Sevim 2004

Study characteristics

Methods	Study design: RCT Setting: orthopaedic outpatient clinics of Mersin University Hospital, Turkey
Participants	**Details of sampling frame:** Total n eligible = not reported Total n excluded pre-randomisation = not reported Total n randomised = 120 participants (120 wrists) Intervention group 1 (proximal injection group) n = 30 wrists

Sevim 2004 *(Continued)*

Intervention group 2 (distal injection group) n = 30 wrists

Intervention group 3 (splint group) n = 60 wrists

Post-intervention follow-up:

Total n available for follow-up = 108 participants (108 wrists)

Total n analysed = 108 participants (108 wrists)

Intervention group 1 (proximal injection group) n = 28 wrists

Intervention group 2 (distal injection group) n = 29 wrists

Intervention group 3 (splint group) n = 28 wrists

Intervention group 4 ("control" group) n = 23 wrists

Gender distribution (reported for participants available for follow-up analysis (n = 108)):

Total: 16 males, 92 females

Intervention group 1 (proximal injection group): 1 male, 27 females

Intervention group 2 (distal injection group): 5 male, 24 females

Intervention group 3 (splint group): 6 males, 22 females

Intervention group 4 ("control" group): 4 males, 19 females

Mean ± SD (range) age (reported for participants available for follow-up analysis (n = 108)):

Total sample: 46.27 ± 10.24 yrs (range 23 to 71 years)

Intervention group 1 (proximal injection group): 43.89 ± 10.54 years (range not reported)

Intervention group 2 (distal injection group): 45.45 ± 11.60 years (range not reported)

Intervention group 3 (splint group): 49.71 ± 9.75 years (range not reported)

Intervention group 4 ("control" group): 46.00 ± 7.90 years (range not reported)

Mean ± SD (range) duration of CTS symptoms:

Total sample: range 5 months to 30 years (mean ± SD not reported)

Inclusion criteria:

1. Referred to the ENMG laboratory for the evaluation of CTS with symptoms including nocturnal paraesthesias, pain in the median nerve distribution during activity, or numbness in the median nerve distribution
2. Abnormal median sensory nerve conduction values

Exclusion criteria:

1. Secondary CTS (i.e. those with diabetes mellitus, hypothyroidism, rheumatic disease, previous wrist trauma)
2. Coincident cervical radiculopathy or ulnar-radial neuropathy
3. Age less than 18 years
4. Previous surgical treatment of CTS, use of splints in the last 6 months, or steroid injections for CTS
5. Median DML longer than 6 ms on ENMG examination
6. Pregnant women
7. People with a median nerve DML longer than the reference values underwent needle EMG of the abductor pollicis brevis muscle, and those with fibrillation potentials, positive sharp waves or chronic

Sevim 2004 *(Continued)*

	neuropathic changes (decreased recruitment pattern, long duration or high amplitude of motor unit potentials) at needle EMG were excluded. 8. Normal motor and sensory conduction values **CTS severity:** Mild-to-moderate
Interventions	Group 1 - **proximal steroid injection** containing 3 mg betamethasone disodium phosphate and 3 mg betamethasone acetate suspension (Celestone Chronodose), mixed with 0.5 cc of a lidocaine HCl solution (Aritmal ampul 2%, 5 cc). The injection site was the volar side of the forearm 4 cm proximal to the wrist crease between the tendons of the radial flexor muscle; the long palmar muscle and the needle was inserted with an angle of 10° to 20° before injection of the solution. All the participants were injected once. Group 2 - **distal steroid injection** containing 3 mg betamethasone disodium phosphate and 3 mg betamethasone acetate suspension (Celestone Chronodose), mixed with 0.5 cc of a lidocaine HCl solution (Aritmal ampul 2%, 5 cc). The needle was inserted at the anterior wrist flexion crease just near to ulnar side of the palmaris longus tendon and angulated 45° distally as well as 45° radially. All the participants were injected once. Group 3 -**splinting** was performed by placing a standard lightweight wrist splint with a metal strip extending across the wrist to the midpalm region. The splint was bent so the wrist would be in neutral position (0° to 5° extended). The participants were instructed to wear the splints every night until the 1-year follow-up (average 11 months, range 9 to 14), and to mark each night that they had worn the splints on a calendar. Group 4 - **control group** formed by the subset of participants who were randomised to the splint group but who did not comply with wearing the splint 6 to 7 days per week during the 1-year treatment period (average 11 months, range 9 to 14), and instead wore the splint less than 1 night per week.
Outcomes	Outcomes assessed at baseline and at the end of 12 months treatment (average of 11 months after the start of treatment, range 9 to 14 months) 1. Neurological symptom score: measured by 2 clinicians using a structured questionnaire regarding possible symptoms of CTS: numbness, pain, paraesthesia, swelling, sense of swelling, drying and/or colour change in the related hand; numbness, pain, paraesthesia of the forearm and arm; provocation of symptoms by housework, reading and driving; existence of night symptoms; awakening due to night symptoms; frequency of night symptoms; numb hand upon awakening in morning; and mean duration of any symptom throughout the day. The severity of each symptom was graded from 0 to 3 (0, no symptom; 1, mild; 2, moderate; 3, severe). The sum of all complaint scores gave a total neurologic symptom score (NSS) for each participant. The authors did not indicate what the possible total NSS was. 2. NCSs: a. median antidromic sensory NCSs of digits I, II and III (m/s) b. ulnar sensory NCS of digit V (m/s) c. median-versus-ulnar digit IV antidromic DSL difference (ms) d. mean antidromic median SNAP amplitude of the 3 digits (digits I, II and III) (uV) e. median MNCV (m/s) f. ulnar MNCV (m/s) g. median second lumbrical-versus-ulnar interossei DML (ms) 3. Adverse effects: the authors did not report how and when adverse effects were recorded.
Funding	Not reported
COI	Not reported
Notes	Of the 60 participants instructed to wear their splints every night, 28 (46.6%) used the splints for an average of 6 to 7 days per week.

Sevim 2004 *(Continued)*

Control group was formed by the subset of participants who were randomised to the splint group but who did not comply with wearing the splint 6 to 7 days per week during the treatment period, and instead wore the splint less than one night per week. We combined data from the splinting and control group (as per ITT principle) and used these combined data in the analyses.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly assigned to one of the 3 groups: splint group (60 patients), distal injection group (30 patients) and proximal injection group (30 patients)." Comment: Not enough information to determine the adequacy of the randomisation sequence generation
Allocation concealment (selection bias)	Unclear risk	Quote: "Patients were randomly assigned to one of the 3 groups: splint group (60 patients), distal injection group (30 patients) and proximal injection group (30 patients)." Comment: Not enough information to determine whether the allocation sequence was adequately concealed until interventions were assigned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Due to the nature of the interventions, participants and personnel were aware of treatment allocations.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Two authors (HK and MA), blinded to the electrophysiologic findings and treatment methods of the patients throughout the study, assessed the patients using a structured questionnaire regarding possible symptoms of carpal tunnel syndrome." Quote: "Electrophysiological examinations were performed on the chosen hand of each patient before and after the treatment, by the same author (SS) who was blinded to treatment methods and historical data throughout the study." Comment: Outcome assessors were probably blind to treatment allocation. However, since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	High risk	Quote: "At the end of 11 months (range, 9 to 14 months), contact with one patient from the proximal injection group and one from the distal injection group were lost for follow-up. Another patient from the proximal injection group refused the electrophysiologic follow-up examination. These 3 patients were dropped from the final analysis. Of the 60 participants in the splint group, 9 wore the splints on average 1-5 nights per week and were excluded. Twenty-three from this group wore the splints less than 1 night per week and were considered to form a control group. The remaining 28 patients wore the splints 6-7 nights per week and they were taken as the properly used splint group. Thus, follow-up evaluation was performed on 28 patients from the proximal injection group, 29 from the distal injection group, 28 from the splint group and 23 from the control group. These 108 participants were re-evaluated by the same methods used at baseline and by the same physicians." Comment: Withdrawals and reasons for these were clearly reported. Participants who did not adhere to the splint protocol were entered into a 'control' group. We combined these participants into the splinting group (as per ITT

Sevim 2004 *(Continued)*

		principle). However, 9 participants were excluded due to not adhering to the treatment and this may have caused bias.
Selective reporting (reporting bias)	Unclear risk	Quote: "The Ethics Committee of Mersin Medical Faculty approved the study protocol." Data for the neurological symptom score (patient self-reported outcome) provided, however, the trial authors did not indicate what the possible total NSS was. The protocol was not available for reading.
Other bias	Low risk	Comment: No other sources of bias identified

So 2018

Study characteristics	
Methods	Study design: prospective, randomised, parallel-group clinical trial Setting: medical clinic of a local hospital (Kwong Wah Hopital), Hong Kong, China.
Participants	**Details of sampling frame:** Total n eligible = not reported Total n excluded pre-randomisation = not reported Total n randomised = 50 Total n available for follow-up = 50 Total n analysed = 50 Intervention group 1 (splint) n = 25 Intervention group 2 (steroid) n = 25 **Gender distribution:** Intervention group 1 (splint): 22 males, 3 females Intervention group 2 (steroid): 21 males, 4 females **Mean ± SD age:** Intervention group 1 (splint): 57.28 ± 9.75 Intervention group 2 (steroid): 57.32 ± 9.12 **Median ± SD duration of CTS symptoms:** Intervention group 1 (splint): 104 weeks (range 39–1040) Intervention group 2 (steroid): 78 weeks (range 12–1040) **Inclusion criteria:** 1. Clinical features: pain, paraesthesia or weakness in the median nerve distribution for at least 3 months **Exclusion criteria:** 1. Inflammatory arthritis 2. Diabetes mellitus

So 2018 *(Continued)*

3. Hypothyroidism
4. Renal failure
5. Polyneuropathy
6. History of significant local trauma
7. Age younger than 18 years
8. Pregnancy
9. Previous treatments of CTS, namely injection, splinting and surgery
10. Motor impairment or thenar muscle atrophy

CTS diagnostic criteria (case definition):

1. Clinical features were pain, paraesthesia or weakness in the median nerve distribution for at least 3 months. The neurodiagnostic criteria were based on the American Academy of Neurology summary statement, which further classified the abnormalities as follows:
   a. mild abnormality, that is, abnormal comparative tests or prolonged median DSL (> 3.5 ms) but normal median DML;
   b. moderate abnormality, that is, prolonged median DSL and DML (> 4.2 ms); and
   c. severe abnormality, that is, absence of median SNAP or absent CMAPs**.**

CTS severity:

Mild, moderate and severe NCV abnormality

Interventions	Group 1 - After randomisation, the hands of the participants in the **splinting group** were splinted in a neutral position with a standard cotton–polyester splint. Participants were instructed to use the splints during night-time for 1 month. Group 2 - the **local injection of steroid** was performed by the same investigator after the randomisation. Using a sterile technique, 20 mg methylprednisolone acetate premixed with lidocaine was injected using a 25-guage 9 5/8" needle. The needle was inserted medially to the palmaris longus tendon at the distal palmar crease in the wrist at an angle of 45° to the forearm. The steroid was injected at approximately 1 cm below the skin. The needle was repositioned if there was any resistance to injection, or any pain or paraesthesia in the median nerve territory.
Outcomes	Outcomes were assessed at baseline and at 4 weeks follow-up. 1. BCTQ symptom severity score (1 to 5; higher is worse) 2. BCTQ functional ability score (1 to 5; higher is worse) 3. BCTQ total change 4. Satisfaction score (1 to 5; higher is better) 5. Nine hole peg test change (seconds; lower is better) 6. Side effects (yes/no) 7. Number changing treatment (crossing over after study period)
Funding	Not reported
COI	The authors reported no conflict of interest.
Notes	The article reported the mean change on the BCTQ Symptom Severity Scale and Functional Status Scale, but the trial author provided end point scores (for Symptom Severity Scale and Functional Status Scale). Participants were encouraged to mark each night they had worn the splints on a calendar to ensure compliance, but results for adherence were not reported.
Risk of bias	

So 2018 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "They were then allocated to one of the two treatment arms according to the randomization procedure using sequentially numbered opaque sealed envelopes (SNOSE). Two sets of [an] equal number of sealed opaque envelopes containing a sheet of paper marked Steroid Injection or Splinting were shuffled very thoroughly. The envelopes were then marked on the front with a unique number sequentially starting from one. Patients were thus randomly assigned to one of the two treatment arms according to what was marked in these envelopes."
Allocation concealment (selection bias)	Low risk	Quote: "They were then allocated to one of the two treatment arms according to the randomization procedure using sequentially numbered opaque sealed envelopes (SNOSE). Two sets of [an] equal number of sealed opaque envelopes containing a sheet of paper marked Steroid Injection or Splinting were shuffled very thoroughly. The envelopes were then marked on the front with a unique number sequentially starting from one. Patients were thus randomly assigned to one of the two treatment arms according to what was marked in these envelopes."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "However, the open label design of the study means the potential ascertainment bias introduced by unblinding is not excluded." Comment: Blinding of participants not attempted
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: Authors did not report any dropouts. Text did not explicitly give numbers in the follow-up but the numbers in the table implied that there were no dropouts.
Selective reporting (reporting bias)	Low risk	Comment: All prespecified outcomes reported. Protocol available
Other bias	Low risk	Comment: Hand used as a unit. There was no apparent source of bias.

Taspinar 2007

Study characteristics	
Methods	Study design: single-blind, randomised, prospectively planned study Setting: Şişli Etfal Training and Research Hospital, İstanbul, Turkey
Participants	**Details of sampling frame:** Total n eligible = 66 Total n excluded pre-randomisation = 31 Total n randomised = 35 (54 hands) Total n available for follow-up = 54 Total n analysed = 54 hands Intervention group 1 (splint) n = 18 hands Intervention group 2 (corticosteroid injection) n = 18 hands Intervention group 3 (physiotherapy) n = 18 hands

Taspinar 2007 *(Continued)*

Gender distribution:

Intervention group 1 (splint): not reported

Intervention group 2 (corticosteroid injection): not reported

Intervention group 3 (physiotherapy): not reported

Total: 0 males, 35 females

Mean ± SD age:

Intervention group 1 (splint): 55.36 ± 7.63

Intervention group 2 (corticosteroid injection): 51.53 ± 9.64

Intervention group 3 (physiotherapy): 53.86 ± 11.52

Total mean: 53.20 ± 9.34

Mean ± SD duration of CTS symptoms:

Intervention group 1 (splint): 4.61 ± 3.39 years

Intervention group 2 (corticosteroid injection): 2.3 ± 2.07 years

Intervention group 3 (physiotherapy): 2.87 ± 2.34 years

Inclusion criteria:

1. Mild-to-moderate EMG findings and no loss of muscle strength in abductor pollicis brevis and opponens pollicis
2. Diabetes mellitus

Exclusion criteria:

1. Polyneuropathy or more proximal compression neuropathy
2. Cervical disc herniation
3. Shoulder, elbow, wrist, finger problems
4. Impingement syndrome
5. Epicondylitis
6. Other aetiological causes of CTS such as a history of fracture
7. de Quervain tenosynovitis
8. Trigger finger
9. Dupuytren's contracture
10. Hypothyroidism
11. Rheumatoid arthritis
12. Gout and other crystal arthropathies
13. Pregnancy
14. Acromegaly
15. Mucopolysaccharidosis
16. Vitamin B12 deficiency
17. Presence of thenar atrophy
18. Previous surgery for CTS
19. Clinical numbness in the feet as well as hands, impaired standing vibration sense, and symptoms suggestive of polyneuropathy
20. Severe CTS

CTS diagnostic criteria (case definition):

Taspinar 2007 *(Continued)*

1. Mild cases: median sensory response latency is long up to 3.5 ms or median sensory response amplitude is low compared to ulnar sensory response amplitude and DML shorter than 5 ms
2. Moderate cases: low median sensory response amplitude or latency longer than 3.5 ms and median DML without findings other than dilution in needle EMG is longer than 5 ms
3. Severe cases: in the abductor pollicis brevis muscle, the median sensory latency is longer than 3.5 ms with signs of neurogenic involvement or the median motor distal response latency is 5 ms and is defined as being longer than the length, low sensory response amplitude or loss of response.

CTS severity:

Mild and moderate EMG findings

Interventions	Group 1 - **splint**: wrist splint with volar support and neutral position made of thermoplastic material, splinting at night for 3 months Group 2 -**steroid injection:** 1 mL Diprospan (5 mg betamethasone dipropionate + 2 mg betamethasone sodium phosphate) Group 3 -**physical therapy:** ultrasound (US) and TENS were applied for a total of 10 sessions, 5 days a week. Continuous US was applied to the volar face of the wrist and the palm at a dose of 1 watt/cm^2 at 1 MHz for 5 minutes. Conventional TENS (slightly above the sensory threshold), negative electrode was placed in the middle of the forearm; positive electrode was placed in the palm and applied for 20 minutes.
Outcomes	Outcomes evaluated before treatment and 3 months after 1. BCTQ symptom severity score (1 to 5; higher is worse) 2. BCTQ functional status score (1 to 5; higher is worse) 3. Pain - VAS 4. Semmes-Weinstein monofilament test 5. Fixed and moving 2-point discrimination test 6. Grip strength (kg) 7. Triple fingertip holding strength 8. Sollerman hand function test (between 0-80) 9. Health Assessment Questionnaire (between 0 and 3) 10. SDL (ms) 11. DML (ms) 12. Motor amplitude (μV)
Funding	Not reported
COI	Not reported
Notes	Written in Turkish; translation used Authors reported that in only one of their participants no steroid-related side effects were observed, however, no clear information regarding side effects in splinting or steroid injection group was reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients included in the study were sequentially randomized into three groups of 18 hands each." Comment: No information about randomisation method provided. The study was planned as a single-blind, randomised, prospective study.

Taspinar 2007 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Comment: No information about allocation concealment provided. The study was planned as a prospective, randomised, single-blind study.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: No information about blinding process provided, but because splinting and steroid injection were obviously different from each other, it is unlikely that the participants were blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: Since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: no dropouts reported and likely all participants had follow-up data but no flow chart provided
Selective reporting (reporting bias)	Unclear risk	Comment: All the outcomes specified in the methods reported, but no study protocol available, therefore unclear
Other bias	Unclear risk	Quote: "A total of 54 hands of 35 patients included in the study were sequentially randomized into three groups of 18 hands each." Comment: Not clear how many participants in each group and no information how the participants with bilateral disease were distributed

Ulucakoy 2020

Study characteristics	
Methods	Study design: single-centre, double-blind, prospective, randomised, placebo-controlled study Setting: Physical Medicine and Rehabilitation outpatient clinic of Ankara Numune Training and Research Hospital, Ankara, Turkey
Participants	**Details of sampling frame:** Total n assessed for eligibility = 323 Total n excluded pre-randomisation = 134 Total n randomised = 189 (295 wrists) Intervention group 1 (splint) n = 47 Intervention group 2 (splint + radial extracorporeal shock wave therapy (rESWT)) n = 47 Intervention group 3 (rESWT) n = 45 Intervention group 4 (splint + placebo rESWT) n = 50 <u>Post-intervention follow-up at 1 month:</u> Total n available for follow-up = 174 (270 wrists) Total n analysed = 174 (270 wrists) Intervention group 1 (splint) n = 42 (67 wrists)

Ulucakoy 2020 *(Continued)*

Intervention group 2 (splint + rESWT) n = 45 (66 wrists)

Intervention group 3 (rESWT) n = 43 (62 wrists)

Intervention group 4 (splint + placebo rESWT) n = 44 (75 wrists)

Post-intervention follow-up at 3 months:

Total n available for follow-up = 168 (259 wrists)

Total n analysed = 168 (259 wrists)

Intervention group 1 (splint) n = 42 (67 wrists)

Intervention group 2 (splint + rESWT) n = 42 (60 wrists)

Intervention group 3 (rESWT) n = 41 (58 wrists)

Intervention group 4 (splint + placebo rESWT) n = 43 (74 wrists)

Gender distribution:

Intervention group 1 (splint): 7 males, 40 females

Intervention group 2 (splint + rESWT): 8 males, 39 females

Intervention group 3 (rESWT): 4 males, 41 females

Intervention group 4 (splint + placebo rESWT): 3 males, 47 females

Mean ± SD age:

Intervention group 1 (splint): 48.1 ± 10.1

Intervention group 2 (splint + rESWT): 48.4 ± 10.1

Intervention group 3 (rESWT): 50 ± 8.6

Intervention group 4 (splint + placebo rESWT): 48.5 ± 9.8

Total mean: 48.8 ± 9.5

Mean ± SD duration of CTS symptoms (months):

Intervention group 1 (splint): 22.2 ± 26.9

Intervention group 2 (splint + rESWT): 33.7 ± 38.1

Intervention group 3 (rESWT): 23.5 ± 27.3

Intervention group 4 (splint + placebo rESWT): 24.8 ± 31.5

Inclusion criteria:

1. Diagnosed with mild-to-moderate CTS

Exclusion criteria:

1. Cervical radiculopathy
2. Brachial plexopathy
3. Polyneuropathy and other upper extremity entrapment neuropathies
4. Previous wrist fracture
5. Cervical spinal and wrist surgeon history

Ulucakoy 2020 *(Continued)*

	6. Steroid injection for CTS 7. Wrist deformity preventing splint use 8. Malign tumoural mass 9. Thrombosis predisposition 10.< 18 years old 11.Pregnancy 12.Receiving dialysis treatment **CTS diagnostic criteria (case definition):** Electrodiagnostic studies **CTS severity:** Mild-to-moderate CTS
Interventions	Group 1: **splint** Group 2: **splint + rESWT** Group 3: r**ESWT** Group 4: **splint + placebo rESWT** In splint groups, a wrist splint with suitable size was advised to be used every night and as much as possible during the day for 3 months. In rESWT groups, the forearm and fingers of the participant were placed on the table with the palm facing up, and median nerve was found with musculoskeletal ultrasonography (US) (LOGIQ® GE Healthcare Ultrasound, Korea). rESWT was performed with the Vibrolith ESWT device (Elmed Medical Systems, Orlando, FL, USA) and the probe was located perpendicularly on the median nerve. The treatment area included the proximal carpal tunnel at the level of the pisiform bone that was shown by transverse US image. The rESWT was applied with 1000 shots, 0.05 mJ/mm^2 intensity of energy and frequency of 5 Hz. The rESWT was administered consecutively for 3 weeks, once a week.
Outcomes	Outcomes evaluated at baseline (pretreatment) and at 1 and 3 months after treatment. 1. BCTQ symptom severity score (1 to 5; higher is worse) 2. BCTQ functional ability score (1 to 5; higher is worse) 3. Pain VAS (from 0 to 10 (0: no pain/paraesthesia, 10: most severe pain/paraesthesia) 4. Finger pinch strength (kg) 5. Leeds Assessment of Neuropathic Symptoms and Signs (0 to 24)
Funding	The authors received no financial support for the research and/or authorship of this article.
COI	The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.
Notes	Outcomes evaluated at baseline (pretreatment) and at 1 and 3 months after treatment, but in analysis, results at 3 months used.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A total of 189 patients (295 wrists) were randomized to four groups by an independent researcher using [a] stratified randomization method. In this randomization, the researcher specified stratification according to the factors (age, sex, and CTS severity) which may affect the outcomes of interven-

Ulucakoy 2020 *(Continued)*

		tion. The patients were, then, assigned to intervention groups using a computer-generated randomization of study numbers."
Allocation concealment (selection bias)	Unclear risk	Quote: "..were randomized to four groups by an independent researcher using [a] stratified randomization method." Comment: No further explanation provided on whether the sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "All interventions were carried out by a single physician who was blinded to the outcome measurements and randomization. Only the sound was heard without energy for placebo rESWT in Group 4 patients." Comment: No information provided about participant blinding, but splinting and ESWT were obviously different from each other, therefore unlikely that the participants were blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "All interventions were carried out by a single physician who was blinded to the outcome measurements and randomization. Only the sound was heard without energy for placebo rESWT in Group 4 patients." Comment: No information about whether participant blinding was provided, but splinting and ESWT were obviously different from each other, therefore unlikely that the participants were blinded.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: All participants were accounted for and reasons for dropout and attrition were documented. Loss to follow-up was 5/47 and 2/45 at one month and 5/47 and 4/45 at 3 months in splint and ESWT groups, respectively. Small and quite balanced loss, not likely to bias the outcomes considerably
Selective reporting (reporting bias)	Unclear risk	Quote: "The study protocol was approved by the Ankara Numune Training and Research Hospital Ethics Committee (No. 829/2016)." Comment: All the outcomes specified in the methods reported, but study protocol was not available for reading, therefore it was unclear.
Other bias	Low risk	Comment: Unit of analysis seemed to be participant, bilateral involvement dispersed evenly between the groups.

Walker 2000

Study characteristics	
Methods	Study design: quasi-randomised controlled trial (prospective, unblinded, randomised clinical trial) Setting: Veterans Administration Medical Center, outpatient clinic
Participants	**Details of sampling frame:** Total n eligible = not reported Total n excluded pre-randomisation = not reported Total n randomised = 21 (30 wrists) Total n available for follow-up = 17 (24 wrists) Total n analysed = 17 (24 wrists) Intervention group 1 (full-time splint) n = 11 wrists (completed the study)

Walker 2000 *(Continued)*

	Intervention group 2 (night-time splint) n =13 wrists (completed the study) **Gender distribution:** Total: 20 males; 1 female (randomised) Intervention group 1 (full-time splint): 7 males; 0 female (completed the study) Intervention group 2 (night-time splint): 9 males; 1 female (completed the study) **Mean ± SD age:** Intervention group 1 (full-time splint): 59.8 ± 9 yrs Intervention group 2 (night-time splint): 60.7 ± 13 yrs Total mean: 60.0 ± 11.2 **Mean ± SD duration of CTS symptoms:** not reported **Inclusion criteria:** 1. Clinical diagnosis of CTS confirmed with electrodiagnostic studies 2. No previous treatment for CTS **Exclusion criteria:** Not reported **CTS diagnostic criteria (case definition):** Electrodiagnostic studies **CTS severity:** Mild, moderate and severe CTS
Interventions	Group 1: **full-time wear of wrist splint** for 6 weeks Group 2: **night-time only wear of wrist splint** for 6 weeks Both groups used custom-made, thermoplastic, lightweight, low-profile, neutral-positioned wrist splint. No work or activity restrictions were given to the participants.
Outcomes	Outcome assessed at the end of six weeks of treatment: 1. BCTQ questionnaire, symptom severity score (1 to 5; higher is worse) 2. BCTQ questionnaire, functional ability score (1 to 5; higher is worse). Nerve conduction: median motor and sensory distal latencies (ms) 3. Compliance (using questionnaire asking whether participants "always/usually wore", "sometimes wore" or "rarely/never wore" splint) 4. NSAID use
Funding	The authors reported that no commercial party having a direct financial interest in the results of the research supporting this article had or would confer a benefit upon the authors or upon any organisation with which the authors were associated.
COI	Not reported
Notes	Strict adherence to specific splint-wearing instructions was reported in 46% of hands, and partial compliance was reported by the remainder. Complete or nearly complete night-time wear of splints was reported by 85% of the night-only group, and by 100% of the full-time group. Complete to near complete daytime wear was reported by only 27% of hands in the full-time group, with the remainder reporting

Walker 2000 *(Continued)*

	partial compliance. Despite instructions for night wear only, 23% of hands in the night-only group reported limited daytime use of splints. One participant in the full-time wear group reported very poor daytime wear compliance because he felt the splints interfered with his job performance.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "The randomization protocol was based on the last digit of the subject's Social Security number." Comment: Allocation sequence was not truly random.
Allocation concealment (selection bias)	High risk	Comment: The last digit of the participant's social security number was used, therefore, allocation was not concealed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: The authors described the trial as "unblinded". Participants were not blinded to splint-wearing. Self-administered questionnaires for the Symptom Severity Scale, Functional Status Scale, and splint-wearing compliance for the last 2 weeks of the trial may have been influenced by the participant's knowledge of their own splint-wearing behaviour.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: Since the outcome assessors for participant-reported outcomes were participants themselves and since it is likely that participants were aware of which treatment they were allocated to, we rated the risk is rated as high.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Quote: "Subjects were informed that steroid injections and surgery were also treatment options for CTS, and participation in this study did not prohibit them from seeking additional treatment, but they would be dropped from the study if they did so". Comment: One participant from each group was excluded because they had surgery or steroid injections. Losses from each group were balanced (2 participants from each group) and unlikely to be a source of bias.
Selective reporting (reporting bias)	Low risk	Comment: All measures appeared to be reported as described in the protocol of the trial publication.
Other bias	Low risk	Quote: "..subjects with bilateral involvement always received the same instructions for both hands...measures were taken for each hand". Comment: Participants were allocated to treatment groups (not hands), therefore, those with bilateral involvement each contributed two hands to the analysis. The number of bilateral cases were similar in both treatment groups, so a unit of analysis error is unlikely to have occurred.

Wang 2017

Study characteristics

Methods	Study design: prospective, single-blind, RCT Setting: Taipei Veterans General Hospital, tertiary care centre
Participants	**Details of sampling frame:** Total n assessed for eligibility = 72

Wang 2017 *(Continued)*

Total n excluded pre-randomisation = 20

Total n randomised = 52 (93 hands)

Total n available for follow-up = 52

Total n analysed = 52

Intervention group 1 (steroid injection + splinting) n = 26

Intervention group 2 (steroid injection) n = 26

Gender distribution:

Intervention group 1 (steroid injection + splinting): 6 males, 20 females

Intervention group 2 (steroid injection): 5 males, 21 females

Mean ± SD age:

Intervention group 1 (steroid injection + splinting): 54.34 ± 9.86

Intervention group 2 (steroid injection): 55.76 ± 8.56

Mean ± SD duration of CTS symptoms:

Intervention group 1 (steroid injection + splinting): 3-6 months, n = 6; 6-12 months, n = 6; 1-2 years, n = 6; > 2 years, n = 8

Intervention group 2 (steroid injection): 3-6 months, n = 5; 6-12 months, n = 7; 1-2 years, n = 5; > 2 years, n = 9

Inclusion criteria:

1. People with typical symptoms of CTS, including nocturnal, postural, or usage associated paraesthesias of the hand
2. Symptoms persisted for at least 3 months before the study
3. Positive Tinel's sign or Phalen's test,
4. Age > 18 years

To confirm the diagnosis of CTS, motor and sensory nerve conduction studies were performed as follows. The electrophysiological tests were considered supportive of CTS when the interval between the median and ulnar sensory peak latencies exceeded 0.5 ms.

Exclusion criteria:

1. Presence of thenar atrophy
2. Existence of disorders such as hypothyroidism, diabetes mellitus, chronic renal failure, or rheumatoid arthritis
3. Any accompanying orthopaedic or neurological disorders that could mimic CTS such as cervical radiculopathy, polyneuropathy, proximal median nerve entrapment, or thoracic outlet syndrome
4. Prior steroid injection into the affected carpal tunnel or carpal tunnel surgery
5. History of the distal radius fracture, pregnancy or lactation
6. Regular use of systemic NSAIDs or corticosteroids
7. Known allergy to corticosteroids and local anaesthetics

CTS diagnostic criteria (case definition):

The electrophysiological tests were considered supportive of CTS when the interval between the median and ulnar sensory peak latencies exceeded 0.5 ms.

CTS severity:

Not reported

Wang 2017 *(Continued)*

	Protocol violators: 2 participants (7.6%) wore the splints 1 to 5 nights/week
Interventions	Group 1 - **steroid injection-plus-splinting group:** Customised volar thermoplastic wrist splint with the wrist placed in a neutral position. Volar splints were made by an experienced occupational therapist. The treating therapist asked participants to wear the splints while sleeping and also during daytime whenever possible for 12 weeks. Group 2 - **steroid injection group:** All participants received a single ultrasound-guided carpal tunnel injection in the affected hand at the beginning of the treatment. Ultrasound-guided injections were given using a 6- to 18-MHz linear array probe. A single physiatrist performed all injections according to the technique described by Smith and colleagues (Smith 2008). The participant was placed in an upright sitting position, with the hand resting on the table, the forearm supinated, and the wrist placed in slight dorsiflexion. The ultrasound probe was placed transversely at the level of the proximal carpal inlet. After sterile preparation, a 25-G, 1.5-in needle was inserted in-plane immediately superficial and lateral to the ulnar artery and directly above and below the median nerve. The injection fluid contained 1 mL of 10 mg (10 mg/mL) triamcinolone acetonide (Shincort) mixed with 1 mL of 2% lidocaine hydrochloride (Xylocaine). Participants were instructed to avoid analgesic/anti-inflammatory drugs for the study period.
Outcomes	Participants were evaluated before the treatment and at 6 and 12 weeks after the onset of treatment. 1. BCTQ symptom severity score (1 to 5; higher is worse) 2. BCTQ functional ability score (1 to 5; higher is worse) 3. BCTQ total (1 to 5; higher is worse) 4. General improvement (6-point Likert-type scale; higher is better) 5. VAS pain (0 to 10; higher is worse) 6. DML (ms; lower better) 7. SNCV (m/s; higher is better), 8. CMAP amplitude (mA; higher is better) 9. SNAP amplitude (mA; higher is better) Compliance with the splint-wearing at night was recorded. Each participant was given a form to record each night he/she wore the splint. The data were collected at 6 and 12 weeks, and the investigator recorded the total number of nights they wore the splint in the 12-week study duration. The average nights per week of splint wear for each participant was calculated.
Funding	Not reported
COI	Not reported
Notes	Of the 26 participants in the steroid injection-plus-splinting group, 24 (92.3%) wore the splints 6 to 7 nights/week. The remaining 2 participants (7.6%) wore the splints 1 to 5 nights/week.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was performed by an independent research assistant who was blinded to treatment and assessment by using a random number generator in blocks of 4 with no stratification."
Allocation concealment (selection bias)	Low risk	Quote: "The allocation of participants to treatment condition was concealed in envelopes, which was opened by a research assistant after the patients' baseline assessment."

Wang 2017 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Based on the nature of the interventions, it was difficult to blind patients." Comment: No blinding was attempted.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Assessments were performed by a physiatrist who was blinded to treatment allocation during the assessments. To ensure blinding, at the beginning of each interview the patients were instructed not to divulge his/her group assignment to the assessors and not to bring the splint with them if patients were assigned to the steroid injection-plus splinting group." Comment: Since participants themselves assessed participant-reported outcomes and they were not blinded, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: No loss to follow-up
Selective reporting (reporting bias)	Low risk	Comment: All the outcomes reported
Other bias	Low risk	Comment: No other sources of bias identified

Werner 2005

Study characteristics	
Methods	Study design: quasi-RCT Setting: a Midwestern auto assembly plant, USA
Participants	**Details of sampling frame:** Total n assessed for eligibility = 2636 Total n excluded pre-randomisation = 2475 Total n randomised = 161 (161 wrists) randomised Intervention group 1 (splint + ergonomic education) n = 86 wrists Intervention group 2 (ergonomic education) n = 75 wrists <u>Post-intervention follow-up:</u> Total n available for follow-up = 112 Total n analysed = 112 Intervention group 1 (splint + ergonomic education) n = 63 wrists Intervention group 2 (ergonomic education) n = 49 wrists **Gender distribution:** Intervention group 1 (splint + ergonomic education): 30 males, 33 females (completed the study)

Werner 2005 *(Continued)*

	Intervention group 2 (ergonomic education): 25 males, 24 females (completed the study) **Mean ± SD (range) age (for those who completed the study):** Intervention group 1 (splint + ergonomic education): 44.74 ± 1.02 (25.6 to 59.0) years Intervention group 2 (ergonomic education): 43.77 ± 1.44 (25.5 to 59.2) years **Mean ± SD duration of CTS symptoms:** Not reported **Inclusion criteria:** 1. Worker-reported symptoms of numbness, tingling, burning, or pain in the wrist or the hand for more than a week or more than 3 times in the last 6 months 2. Hand diagram was suggestive of CTS; that is, there were symptoms of numbness, tingling, burning, or pain in the median nerve distribution. **Exclusion criteria:** 1. Upper-extremity musculoskeletal disorders secondary to acute trauma on or off the job 2. History of bilateral carpal tunnel release surgery 3. Pregnancy **CTS diagnostic criteria (case definition):** Study examined the efficacy of splints among participants with symptoms consistent with CTS, but not necessarily having the diagnosis established. **CTS severity:** Not reported
Interventions	Group 1 - **splint + ergonomic education**: Customised wrist splints and ergonomic education - participants were fitted with a custom wrist-hand orthosis that maintained the wrist in a neutral posture, and was worn at night for 6 weeks. Participants received instructions in how to reduce ergonomic stressors in the work and home environments by viewing a 20-minute video on CTS and ergonomic risk factors. The focus of the video was industrial ergonomics and the prevention of repetitive strain disorders. Group 2 -**ergonomic education alone**: Ergonomic education alone via the same 20-minute video on CTS and ergonomic risk factors presented to participants in the intervention group
Outcomes	Outcomes assessed at baseline, and 3, 6, and a mean of 12 months (range 7 to 15 months) follow-up (after the end of treatment) 1. BCTQ Symptom Severity Scale (1 to 5; higher is worse) 2. Elbow and forearm, and wrist, hand and finger discomfort using a 30-day worst-discomfort rating on a 0 to 10 VAS 3. Surgical rates for CTS 4. Nerve conduction: median nerve sensory peak latency (msec), median nerve sensory amplitude (μv), median-ulnar peak latency difference (msec) 5. Data in Occupational Health and Safety administration logs, plant medical records, disability records, days of work missed due to upper extremity problems, and workers' compensation status or work restrictions collected from computerised records 6. Splint usage and satisfaction (only in the intervention group) using a questionnaire administered at the end of the 6-week treatment period
Funding	Supported in the whole by joint funds from the United Auto Workers (UAW) and General Motors (GM) National Joint Committee on Health and Safety

Werner 2005 *(Continued)*

	"No commercial party having a direct interest in the results of the research supporting this article has or will confer a benefit on the author(s) or on any organization with which the author(s) is/are associated."
COI	Not reported
Notes	According to the trial authors, half the participants did not complete the questionnaires at 3-month and 6-month follow-up, so no data from these time points were reported. The authors did not report numbers regarding adherence to splint use.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Subjects were randomized to either a treatment or a control group, depending on whether the last digit of their Social Security number was odd or even." Comment: The trial authors used a non-random component in the sequence generation process.
Allocation concealment (selection bias)	High risk	Quote: "Subjects were randomized to either a treatment or a control group, depending on whether the last digit of their Social Security number was odd or even. Subjects were not informed of the sequence for random allocation nor were they told to which group they were assigned until after consenting to participate." Comment: The trials authors did not adequately conceal the treatment allocation until interventions were assigned, as a non-random process was used.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Subjects were not blinded to their treatment, and the primary outcome measure was a self-reported symptom severity score." Comment: Participants were not blinded to treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The nerve conduction data were collected at baseline and at the 12-month follow-up. Subjects reported to the medical department to have the testing done during regular work hours, and the person doing the testing was blinded to the treatment assignment." Comment: Since participants themselves assessed participant-reported outcomes and they were likely to be aware of their allocated treatment in this study, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	High risk	Quote: "Data collection was incomplete at the 3- and 6-month follow-up periods. Subjects were contacted by a study site coordinator and were reminded to fill out the questionnaire, but about half of the subjects did not complete the 3- or 6-month questionnaires. The trend in outcome measures at 3 and 6 months was similar to the results at 12 months." Comment: Data not complete for all outcomes, with no explanation as to how this may have impacted on the data reported
Incomplete outcome data (attrition bias) After 3 months	High risk	Quote: "The 12-month follow-up data are presented because they represent a more complete data set...The 12-month follow-up was actually a range of follow-up times, with an average of 12 months and a range of 7 to 15 months." Comment: Data not complete for each outcome, with no explanation as to how this may have impacted on the data reported

Werner 2005 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Comment: The results of participant self-reported outcomes reported; however, protocol not available
Other bias	Low risk	Comment: No other sources of bias identified

Willis 2016

Study characteristics	
Methods	Study design: Unblinded RCT Setting:
Participants	**Details of sampling frame** Total n eligible = 60 Total n excluded pre-randomisation = 10 Total n randomised = 50 Total n available for follow-up = 50 Total n analysed = 50 Intervention group 1 (splint) n = 25 Intervention group 2 (control) n = 25 **Gender distribution** Intervention group 1 (splint): 7 males; 18 females Intervention group 2 (control): 3 males; 22 females **Mean ± SD (range) age** Intervention group 1 (splint): not reported Intervention group 2 (control): not reported Total: 51 ± 12.6 **Mean SD (range) duration of symptoms** Not reported **Inclusion criteria** 1. One of the following symptoms of CTS: numbness, tingling, or pain in the wrist or hand 2. ≥ 18 years old and of either gender 3. Agree and be able to sign a voluntary consent to participate form 4. NCS results are as follows: a. Sensory conduction latency to peak greater than 3.7 ms when measured with ring pick up on the volar surface of the index finger measured 14 cm from stimulation across the wrist at the median nerve b. Motor conduction latency to take off greater than 4.2 ms when measured with disc pick up on the abductor pollicis brevis muscle measured 8 cm from stimulation across the wrist at the median nerve **Exclusion criteria** 1. Thenar atrophy of the hand 2. Currently undergoing manual hand therapy 3. Previously diagnosed with cervical radiculopathy 4. Evidence of a “double crush” syndrome 5. Pregnancy

Willis 2016 *(Continued)*

6. Ganglion cyst of the wrist
7. NCS results as follows:
   a. Sensory conduction latency to peak less than 3.7 ms when measured with ring pick up on the volar surface of the index finger, measured 14 cm from stimulation across the wrist at the median nerve
   b. Motor conduction latency to take off less than 4.2 ms when measured with disc pick up on the abductor pollicis brevis muscle measured 8 cm from stimulation across the wrist at the median nerve

CTS diagnostic criteria (case definition)

Physical examination and a NCS of the median nerve following electrodiagnostic standards established by the American Association for Hand Surgery

CTS severity:

Not reported

Interventions	Group 1 - **splint:** The participants were treated with **Dynasplint stretching modality**. Participants wore the device for two 30-minute sessions per day with regular increases in splint tension for 60 days. Each Dynasplint was customised by one technician to fit each participant's hand length, width, and girth. The first week of Dynasplint use was an accommodation period for the participant, and participants were encouraged to wear the unit twice daily for 15 minutes each session. Time was then increased by 2 to 4 minutes each following session. After the participant comfortably wore the device for two 30-minute sessions each day for 1 week, instructions were given to increase the tension of the Dynasplint device once every 2 weeks, based on comfort and tolerance. If the new tension setting caused excess joint fatigue or "soreness," the participant was instructed to reduce the time to 15 minutes, twice daily, and work the time back up to 30 minutes, twice daily. The goal was to wear the modality for 30 minutes, twice a day and increase the tension twice a month, based on comfort and tolerance. All participants were instructed to communicate on compliance through weekly transfer of wearing diary records to the prescribing physician. Group 2 - **control:** The control participants were only treated with **NSAIDs**, **stretching exercises**, and **instructions** for reducing the potential movement causing the pain. Steroid injections were not given.
Outcomes	The outcomes were assessed at 2 months (BCTQ score) and at 12 months (rate of surgery). 1. BCTQ score (modified scale 0 to 100; higher score indicates worse state) 2. Number/proportion chosen/having surgery at 12 months follow-up
Funding	The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: funding to operate Galveston Clinical Research is obtained through book revenues, allowing this to be completely independent research.
COI	The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: "Neither author has conflict of interest at this time. Neither author has received any earnings or compensation for this publication; nor will any earnings be awarded in the future. Dr. F.B.W. was employed by Galveston Clinical Research Foundation at the time of this study. He had a previous affiliation with the parent company of Dynasplint Systems, Inc. but the affiliation including all compensation or earnings were completed in 2013. B.F. was previously employed by Dynasplint Systems but her employment was also completed in 2013."
Notes	BCTQ score scale is normally from 1 to 5. The authors have used a modified version "The Levine-Katz survey used in the study measures symptoms in two categories, totaling 100 points." The trial reported 100% compliance over 60 days and after completion of the controlled trial, treatments over the second phase (12 months) were intentionally unregulated but were tracked.

Willis 2016 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly assigned to either the experimental or control group". Comment: No further description of the random sequence generation
Allocation concealment (selection bias)	Unclear risk	Comment: It was not clear if concealment of allocation was achieved.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Participants were not blinded to the allocation.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: Because it is likely that participants were aware of which treatment they were allocated to, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: 100% follow-up rate at 2 months but data incompletely reported
Incomplete outcome data (attrition bias) After 3 months	Low risk	Comment: 100% follow-up data reported (but only for the rate of surgery)
Selective reporting (reporting bias)	High risk	Comment: Partial reporting; at long-term follow-up, the authors reported only surgery rates, and at short-term follow-up no scores.
Other bias	High risk	Comment: Corresponding author is an employee of Dynasplint Systems, Inc.

Wu 2017

Study characteristics

Methods	Study design: prospective, single-blinded, RCT Setting: Tri-Service General Hospital, Taiwan
Participants	**Details of sampling frame:** Total n assessed for eligibility = 80 Total n excluded pre-randomisation = 20 Total n randomised = 60 Total n available for follow-up = 60 Total n analysed = 60 Intervention group 1 (splint) n = 30 Intervention group 2 (platelet-rich plasma (PRP)) n = 30 **Gender distribution:**

Wu 2017 *(Continued)*

	Intervention group 1 (splint): 5 males; 25 females Intervention group 2 (PRP): 3 males; 27 females **Mean ± SD age:** Intervention group 1 (splint): 54.27 ± 7.34 Intervention group 2 (PRP): 57.87 ± 8.27 **Mean ± SD duration of CTS symptoms (months):** Intervention group 1 (splint): 30.70 ± 33.0 Intervention group 2 (PRP): 34.43 ± 31.1 **Inclusion criteria:** Paraesthesia or dysaesthesia, painful swelling with clumsy weakness of the hand exacerbated by sleep or repetitive use of the wrist, and relieved by shaking the hand with postural change, AND 1 or more of the following: 1. Sensory loss with numbness in the median nerve-innervated regions of the hand 2. Weakness with atrophy of the median nerve-innervated thenar muscles 3. Positive Phalen's test and Tinel's sign, or both Participants diagnosed with mild-to-moderate unilateral CTS with clinical symptoms for at least 3 months undergoing electrophysiological study and ultrasonography were enrolled. **Exclusion criteria:** 1. History of wrist surgery, polyneuropathy, brachial plexopathy, or thoracic outlet syndrome 2. History of thrombocytopenia, platelet dysfunction, systematic infection, pregnancy, and rheumatologic disorders 3. Previous steroid injection for CTS **CTS diagnostic criteria (case definition):** The cut-off points or normal range of the electrophysiological study for CTS in this study were as follows: 1. upper limit of the median nerve SDL is ≤ 3.6 ms at a distance 14 cm away from the active recording 2. difference in SDL between the ulnar and median nerve is < 0.4 ms and 3. upper limit of DML of the median nerve is < 4.3 ms at a distance 8 cm away from the thenar muscle belly Participants with mild and moderate CTS were categorised by the electrophysiological classification of CTS by Padua and colleagues (Padua 1997): mild: only abnormal digit/wrist SNCV with normal DML; moderate: abnormal digit/wrist SNCV and abnormal DML; or severe: absence of SNCV and abnormal DML. **CTS severity:** Mild-to-moderate CTS
Interventions	Group 1 - **received a night splint through the study period:** The splint was applied in a neutral position to restrict the wrist as previously described. The controls were instructed to put on the splint overnight for at least 8 hours daily throughout the study period. Group 2 - **PRP group:** participants were injected with one dose of 3 mL of PRP using ultrasound guidance. Ten mL of blood sample were drawn from the antecubital vein using RegentKit-THT-1 (RegenLab SA, Mont-sur-Lausanne, Switzerland) followed by centrifugation at 3400 rpm for 15 minutes at room temperature using Regen Lab PRP Centri, yielding 3.5 mL of PRP. The RegentKit-THT-1 has sodium citrate solution as an anticoagulant, and autologous thrombin as an activator to advance platelet acti-

Wu 2017 *(Continued)*

	vation and conversion of fibrinogen to fibrin. For quality tests, 0.5 mL of the PRP sample was sent to the laboratory and 3 mL was used for the ultrasound-guided injection. The concentration of platelets and leukocytes in the PRP was approximately 2.7 ± 0.4 times and 1.2 ± 0.4 times that in whole blood, respectively. The ultrasound-guided PRP injection was performed by the same physiatrist, using ultrasonography (MyLab™ 25Gold, Esaote, Genova, Italy). With the palm facing upwards and the wrist slightly extended, the median nerve was identified at the inlet of the proximal carpal tunnel (pisiform level). The ultrasound-guided injection was conducted using the in-plane ulnar approach. The ulnar artery was identified using Doppler imaging, and a 25-gauge needle was passed from the ulnar side of the wrist toward the median nerve. After placing the needle tip on the median nerve, 2 mL of PRP was injected to peel the nerve off the flexor retinaculum via hydrodissection. An additional 1 mL of PRP was delivered to the inferior part of the median nerve and the median nerve was peeled from the underlying subsynovial connective tissue. After this, the entire carpal tunnel was scanned to ensure that the PRP had spread throughout the proximal-to-distal area of the carpal tunnel. **Both groups**: All participants were instructed to refrain from any other management approaches, such as analgesics, steroid injections, or physical therapy, for CTS symptoms from 2 weeks before and throughout the study period, and were requested to report receiving any of these therapies.
Outcomes	Outcomes were assessed before intervention and at months 1, 3, and 6 after treatment 1. BCTQ Symptom Severity Score (1 to 5; higher is worse) 2. BCTQ Functional Status Score (1 to 5; higher is worse) 3. Pain severity and paraesthesia, VAS (0 to 10; higher is worse) 4. Cross sectional area median nerve (mm^2) 5. SNCV (m/s; higher is better) 6. DML (ms; lower is better) 7. Finger pinch strength (kg; higher is better) 8. Adverse events
Funding	The study is supported by the Ministry of Science and Technology, Taiwan, Republic of China (grant no. MOST 105-2314-B-016-046).
COI	The authors declared that they had no competing interests.
Notes	Results from BCTQ not reported in scale 1 to 5. We assumed that the total sum was reported and divided the symptom score by 11 and functional score by 8 (as per instructions of the scale). Authors reported standard error (SE) for age and duration of symptoms, but we calculated SD (SE * SQRT n).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The enrolled patients were block randomized in a 1:1 ratio into two groups, control and PRP groups, by an independent researcher via computer-generated randomization of study numbers (Microsoft Excel, Microsoft Inc., Redmond, WA, USA)."
Allocation concealment (selection bias)	Unclear risk	Comment: The method of allocation concealment not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Blinding of participants not attempted

Wu 2017 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "One physiatrist (Dr. Ke) with 5 years' experience in musculoskeletal ultrasonography and electrophysiological study, who was blinded to the patients' randomization, performed all the measurements in all patients of both groups before intervention and at months 1, 3, and 6 after treatment." Comment: However, as the participants were likely aware of which treatment they were allocated to, we rated the risk as high.
Incomplete outcome data (attrition bias) 3 months or less	Low risk	Comment: No loss to follow-up
Incomplete outcome data (attrition bias) After 3 months	Low risk	Comment: No loss to follow-up
Selective reporting (reporting bias)	Unclear risk	Comment: According to the protocol, outcomes were assessed at 1, 2, 4, 8, 12, 16 and 24 weeks. Results reported at 1, 3 and 6 months. Unclear if this was related to the nature of the findings
Other bias	Low risk	Comment: No other sources of bias identified

Yazdanpanah 2012

Study characteristics	
Methods	Study design: RCT Setting: S. Mofateh Clinic, Iran
Participants	**Details of sampling frame:** Total n eligible = 28 Total n excluded pre-randomisation = not applicable Total n randomised = 28 Intervention group 1 (splint) n = 14 Intervention group 2 (steroid injection) n = 14 <u>Post-intervention follow-up:</u> Total n available for follow-up = 25 Total n analysed = 25 Intervention group 1 (splint) n = 11 Intervention group 2 (steroid injection) n = 14 **Gender distribution:** Intervention group 1 (splint): 0 males, 14 females Intervention group 2 (steroid injection): 0 males, 14 females **Mean ± SD age:**

Yazdanpanah 2012 *(Continued)*

	Total: range between 26 to 49 years, and among them the range of 28-31 years had the most frequency **Mean ± SD duration of CTS symptoms:** Not reported **Inclusion criteria:** 1. Paraesthesia of hands in duration of pregnancy 2. Severe CTS **Exclusion criteria:** 1. Diabetes mellitus 2. Collagen vascular disease 3. Renal failure 4. Hypothyroidism, 5. Rheumatoid disease 6. Pre-pregnancy CTS 7. Positive family history of neuropathy 8. Carpal tunnel surgery 9. Fracture of wrist bones **CTS diagnostic criteria (case definition):** 1. Electrodiagnostic evaluation of CTS: a. A difference of greater than 0.5 ms between the median and ulnar nerve sensory latencies in the same hand b. A difference of greater than 1 ms between the median and ulnar motor latencies in the same hand Severity of CTS was based on neurophysiology findings and guideline values of the Association of the Electrodiagnostic Medicine.
Interventions	Group 1 - **splint**: Splint in neutral position during night for 6 weeks (wrist splint made by Iran Odor Company in Iran) Group 2 - **steroid injection**: triamcinolone (Triamhexal) 40 mg; made by Holzkirchen factory in Germany, was injected without anaesthetic substance and using needle number 23, with 30° angle on radial side of wrist in carpal tunnel.
Outcomes	Outcomes were evaluated before treatment and 2 months after treatment. Electrophysiologic parameters of median and ulnar nerves were recorded before and 2 months after the steroid injection and wrist splint. The effectiveness of treatment was described in the manner of 1) **change of disease stage** from severe to moderate or mild or 2) **complete recovery**. In cases of observing changes from severe to lower stages of the disease in electrodiagnostic studies, treatment was considered successful and otherwise failed.
Funding	Not reported
COI	Not reported
Notes	Inclusion criteria were: If a pregnant woman had severe CTS, she was entered in the research. Nevertheless, in the results the authors reported that participants had varying severity of CTS.

Risk of bias

Bias	Authors' judgement	Support for judgement

Yazdanpanah 2012 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "Then, the patients were randomly placed in one of treatments groups including steroid injection and wrist splint treatments." Comment: No further information about the sequence generation provided
Allocation concealment (selection bias)	Unclear risk	Comment: No information about allocation concealment provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: No information about blinding provided. Splinting and steroid injection were obviously different from each other, therefore, unlikely that the participants were blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: No information about blinding provided. Splinting and steroid injection were obviously different from each other, therefore, unlikely that the participants were blinded.
Incomplete outcome data (attrition bias) 3 months or less	High risk	Quote: "Three women in splint group refused to continue treatment". Comment: This corresponded to 21% loss in one group and no loss in the other.
Selective reporting (reporting bias)	Unclear risk	Comment: No protocol or registration provided. Only electrodiagnostic studies reported and unclear if clinical outcomes measured
Other bias	Unclear risk	Comment 1: All participants were pregnant. It was unclear if pregnancy is an effect modifier. Comment 2: Randomisation done at participant level, but unit of analysis was hand. Not clear how the participants with bilateral disease were distributed, also not clear information if all 50 studied hands actually were affected by CTS or not. Quote: "Among the studied women, 5 (20 percent) were suffering in the left hand, 14 (56%) in the right hand and 6 (24%) in both hands. In view of severity of CTS among 50 studied hands, 31 (62%) were suffering from severe CTS, 6 hands (12%) were normal from the beginning. Also among 50 hands, 9 (18%) were in mild CTS and 4 hands (8%) were in moderate stage of CTS."

ASHT: American Society of Hand Therapists
BCTQ: Boston Carpal Tunnel Questionnaire
CMAP: compound motor action potential
CTS: carpal tunnel syndrome
CTSAQ: Carpal Tunnel Syndrome Assessment Questionnaire
DML: distal motor latency
DN4: Douleur Neuropathique en 4 Questions-questionnaire
DSL: distal sensory latency
E(N)MG: electro(neuro)myography
EQ-5D-5L: EuroQol 5-dimension 5-level health status and quality of life measure
EuroQol: EuroQol Groupt
GP: general practitioner
HCl: hydrochloric acid
IQR: interquartile range
ITT: intention-to-treat
KT: kinesiotaping
Lp: placebo laser
Lv: real laser
M(N)CV: motor (nerve) conduction velocity
MRI: magnetic resonance image
na: not available
NCS: nerve conduction study

NCV: nerve conduction velocity
NSAID: nonsteroidal antiinflammatory drug
NSS: Neurologic Symptom Score
OD: orthotic device
PI: principal investigator
RCT: randomised controlled trial
rESWT: radial extracorporeal shock wave therapy
rpm: rounds per minute
SD: standard deviation
SDL: sensory distal latency
SE: standard error
SNAP: sensory nerve action potential
SNCV: sensory (nerve) conduction velocity
SNOSE: sequentially numbered opaque sealed envelopes
SQRT: square root
TENS: transcutaneous electrical nerve stimulation
US: ultrasound
VAS: visual analog scale

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Akalin 2002	The same type of splint was applied to each group in this trial.
Arinci Incel 2005	Study compared treatment methods which we defined as not relevant for this review.
Asgari 2020	Splint applied to each group in this trial
Bagheri 2011	Splint applied to each group in this trial
Baker 2012	Splint applied to each group in this trial
Bardak 2009	The effect of splinting could not be isolated from that of the other intervention delivered alongside it.
Baysal 2006	The same type of splint was applied to each group in this trial.
Bilgici 2010	The effect of splinting could not be isolated from that of the other intervention delivered alongside it.
Brininger 2007	Splint applied to each group in this trial
Bulut 2015	Splint applied to each group in this trial
Burke 1994	Splint applied to each group in this trial
Bye 2011	Splint applied to each group in this trial
Celiker 2002	The effect of splinting could not be isolated from that of the other intervention delivered alongside it.
Chung 2016	Splint applied to each group in this trial
CTRI/2015/02/005531	Splint applied to each group in this trial
Daniel 2000	Not a randomised trial

Study	Reason for exclusion
Davis 1998	The same type of splint was applied to each group in this trial.
De Angelis 2009	Splint applied to each group in this trial
Dehghani 2012	Splint applied to each group in this trial
Dincer 2009	Splint applied to each group in this trial
DRKS00014585	Study compared treatment methods which we defined as not relevant for this review.
Eftekharsadat 2011	The same type of splint was applied to each group in this trial.
Ekim 2008	The same type of splint was applied to each group in this trial.
Evcik 2007	The same type of splint was applied to each group in this trial.
Farahmand 2021	Splint applied to both study groups
Garfinkel 1998	Study compared treatment methods which we defined as not relevant for this review.
Garland 1964	Study compared treatment methods which we defined as not relevant for this review.
Gerritsen 2002	Study compares treatment methods which we defined as not relevant for this review
Golriz 2016	Study compared two types of splint.
Gurcay 2009	The same type of splint was applied to each group in this trial.
Halac 2015	Not a randomised trial
Heebner 2008	The same type of splint was applied to each group in this trial.
Hojjati 2020	Splint applied to each of the study groups
IRCT2012122811912N1	The effect of splinting could not be isolated from that of the other intervention delivered alongside it; study compared treatment methods that we defined as not relevant for this review.
IRCT20130612013651N4	Splint applied to each group in this trial
IRCT2013092612450N1	Splint applied to each group in this trial
IRCT2014083118991N1	Splint applied to each group in this trial
IRCT201412014641N9	The effect of splinting could not be isolated from that of the other intervention delivered alongside it.
IRCT20190429043421N1	Splint applied to each group in this trial
IRCT20201130049540N1	Splint seemed to be applied in both interventions.
Kamanli 2011	The same type of splint was applied to each group in this trial.
Khosrawi 2012	Splint applied to each group in this trial
Koca 2014	Study compared treatment methods which we defined as not relevant for this review.

Study	Reason for exclusion
Krause 2020	The effect of splinting could not be isolated from that of the other intervention delivered alongside it.
Kumnerddee 2010	Study compared treatment methods which we defined as not relevant for this review.
Lewis 2020	The effect of splinting could not be isolated from that of the other intervention delivered alongside it.
Luong 2017	Not a randomised controlled trial
Mansiz Kaplan 2018	Splint applied to each group in this trial
Mohammadabadi 2018	Splint applied to each group in this trial
NCT04043780	Splint applied to each group in this trial
NCT04416867	Splint applied to each of the study groups
NCT04733209	The effect of splint could not be isolated from the co-interventions delivered with it.
Pinar 2005	The same type of splint was applied to each group in this trial.
Politis 2015	Splint applied to each group in this trial
Raeissadat 2014	Splint applied to each group in this trial
Raji 2019	The effect of splinting could not be isolated from that of the other intervention delivered alongside it.
Rayegani 2013	Splint applied to each group in this trial
Roitberg 2003	Not a randomised controlled trial (the article was a commentary)
Ruksen 2011	The same type of splint was applied to each group in this trial.
Salehi 2019	Splint applied to each group in this trial
Setayesh 2017	Study compared treatment methods which we defined as not relevant for this review.
Šošić 2020	Splint applied to each group in this trial
Soyupek 2012	Study compared treatment methods which we defined as not relevant for this review.
Storey 2013	Splint applied to each group in this trial
Talebi 2013	Splint applied to each group in this trial
Toopchizadeh 2020	Splint applied to each group in this trial
Ucan 2006	Study compared treatment methods which we defined as not relevant for this review; splint applied to each group
Weintraub 2000	The effectiveness of a wrist support strap (not a splint) was investigated in this study.
Weng 2016	Not a randomised trial

Study	Reason for exclusion
Yao 2019	Not a randomised trial
Zhang 2018	Study compared treatment methods which we defined as not relevant for this review; the effect of splinting could not be isolated from that of the other intervention delivered alongside it.
Zinnuroglu 2010	Splint applied to each group in this trial

Characteristics of studies awaiting classification *[ordered by study ID]*

Baklaci 2015

Methods	Study design: Prospective, randomised, placebo-controlled clinical study
Participants	**Details of sampling frame:** Total n = 80 participants Group 1 (physical therapy) n = 21 Group 2 (splinting) n = 22 Group 3 (physical therapy + splinting) n = 18 Group 4 (placebo (sham) physical therapy) n = 19 **Gender distribution:** Total: 78 female, 2 male **Duration of CTS symptoms:** Not reported **Inclusion criteria:** People with CTS **Exclusion criteria:** Not reported
Interventions	Group 1: Physical therapy - steroid iontophoresis using dexamethasone as a conductive agent (500 g/mol, 2.5 mA–4 mA), continuous ultrasound at 2.0 W/cm^2 (3 MHz, 4 cm^2 probe area), paraffin bath for hands was applied to the physical therapy group for 15 sessions. Group 2: Lightweight, neutral positioned wrist splint was applied to the 2nd group for 1 month (24 hours a day). Group 3: Both physical therapy and splinting were applied to the 3rd group in the same way and for the same duration as 1st and 2nd groups. Group 4: Placebo (sham) ultrasound and placebo (sham) iontophoresis without steroid (both without energy emission) were applied to the sham therapy group.
Outcomes	Outcomes evaluated at baseline after the treatment and at 1st, 3rd and 6th 1. Electroneurophysiological parameters (DML, motor amplitude, SNCV, sensory peak latency and sensory amplitude of median nerve) 2. BCTQ

Baklaci 2015 *(Continued)*

Notes	Report available only as a conference abstract

Bhuva 2019

Methods	Study design: unclear (awaiting information from the authors)
Participants	**Details of sampling frame:** Total n analysed = 26 (30 wrists) **Gender distribution:** Total: 7 males, 19 females **Duration of CTS symptoms:** 2 to 5 months **Inclusion criteria:** 1. Nocturnal pain 2. Numbness 3. Paraesthesias 4. Tingling in the region of hand, especially in the thumb, index and middle fingers 5. Subjective symptoms test 6. Either positive carpal compression test or Phalen's test **Exclusion criteria:** 1. Open wound or skin disease 2. Hand surgery 3. Traumatic condition 4. Wrist fracture 5. Infection 6. Thyroid disease 7. Diabetes mellitus
Interventions	Group 1: Customised splint, ultrasound and exercises (splint to wear every night for 4 weeks) Group 2: Soft tissue mobilisation, ultrasound, exercises
Outcomes	Outcomes evaluated at baseline and post-treatment (after 4 weeks) 1. VAS 2. BCTQ Functional Status Scale
Notes	Email sent to the authors but no response. Unclear if randomised trial or not

IRCT2014020416485N1

Methods	Study design: Randomised, not blinded, parallel-group, placebo-controlled Setting: Baqiyatallah University of Medical Sciences polyclinic and University of Social Welfare and Rehabilitation Sciences affiliated clinics

IRCT2014020416485N1 *(Continued)*

Participants	**Details of sampling frame:** Target sample size: 150 **Gender:** Both **Age:** No age limit **Duration of CTS symptoms (N of participants):** **Inclusion criteria:** People with mild to moderate CTS with no history of surgical and local steroid injection, any age or gender **Exclusion criteria:** Severe CTS and severe dysfunction that needs surgical median nerve release History of other therapeutic approaches History of allergy against steroids or triamcinolone Steroid contraindications History of cardiac arrhythmia Diabetes mellitus Hand surgeries in past 3 months Rheumatoid arthritis Cervical radiculopath Thyroid dysfunctions
Interventions	Group 1: injection of 80 mg triamcinolone with 1 mL lidocaine 2% by hydrodissection method Group 2: injection of 40 mg triamcinolone with 1 mL distilled water and 1 ml lidocaine 2% by hydrodissection method Group 3: injection of 2 mL distilled water and 1 mL lidocaine 2% by hydrodissection method Group 4: injection of 40 mg triamcinolone without hydrodissection method Group 5: wrist splinting for 6 weeks
Outcomes	1. BCTQ score 2. Median nerve ultrasound study 3. Median nerve conduction study 4. Pain score
Notes	Recruitment complete

ISRCTN22916517

Methods	Study design: Randomised, open cross-over study

ISRCTN22916517 *(Continued)*

	Primary study design: interventional Secondary study design: RCT Trial setting: not specified
Participants	Participant inclusion criteria: 80 participants in total: 40 with primary CTS and 40 with secondary CTS Participant type: patient Age group: not specified Gender: not specified Target number of participants: 80 Participant exclusion criteria: not provided at time of registration
Interventions	Wrist splints versus steroid injection
Outcomes	Primary outcome measure: proportion of participants improved at 6 weeks Secondary outcome measures: VAS for pain and tingling, grip strength test, adverse effects of treatment, recurrence or surgery within 12 months
Notes	Overall trial status: completed (12 September 2003) Recruitment status: no longer recruiting (12 September 2003) Publication status: results overdue (20 August 2015)

Riasi 2015

Methods	Study design: unclear (awaiting information from the authors) Setting: neurology clinic of Vali Asr Hospital of Birjand
Participants	**Details of sampling frame:** Total n analysed = 40 participants (wrists) **Gender distribution:** Total: 10 males, 30 females Age: 32.75 ± 4.33 years (ranging from 20 to 48 years) **Duration of CTS symptoms:** CTS diagnosis confirmed based on clinical examinations (Phalen's and Tinel's sign) and a proximal and distal amplitude difference higher than 50% and delayed distal motor conduction velocity lower than 20 m/s **Inclusion criteria:** 1. Personal consent of the participants 2. Participants must not be pregnant at the time of entering the study, and their condition must not be the result of maternity and pregnancy 3. Participant's CTS should not be a complication of tumours in the carpal region or a result of trauma or fracture to the carpal bones

Riasi 2015 *(Continued)*

	4. Participant should not have suffered from the cellular damage of the upper limb or their spine before entering the study 5. Participants must not have any history of substance abuse 6. No signs of denervation should come up in the EMG scan results of the participants. Also, their condition should not have led to other complications such as thenar atrophy 7. Participant's condition must not be the result of rheumatoid arthritis or other collagen vascular disorders 8. The participant's condition must not be the result of metabolic disorders such as diabetes or disorders of the thyroid gland 9. Participants must be conscious to a degree which enables them to partake in follow-up studies and comply with their physicians' necessary recommendations **Exclusion criteria:** 1. Absence in follow-up re-examinations and clinical tests 2. Specific organic pathological disorders such as cancers, tumours, fractures, and collagen vascular diseases such as rheumatoid arthritis, metabolic diseases such as diabetes, thyroid disorders, or other problems that may be disruptive in the study process
Interventions	Group 1: ibuprofen (800 mg twice daily for 4-6 weeks) with a short wrist splint Group 2: ibuprofen (800 mg twice daily for 4-6 weeks)
Outcomes	Outcomes evaluated at baseline and after 4 to 6 weeks of treatment NCV and EMG examinations
Notes	Email sent to the authors, awaiting response. Unclear if randomised trial or not

Soon 2015

Methods	Single-blinded, randomised clinical trial with a 2 × 2 factorial design Setting: university clinical research centre and a network of clinical practices
Participants	Total n = 120 participants Group 1 (splint + multimodal approach comprising of manual mobilisation techniques, education and nerve and tendon gliding exercises (MEX)) n = 30 Group 2 (splint + ultrasound) n = 30 Group 3 (MEX alone) n = 30 Group 4 (ultrasound alone) n = 30 **Inclusion criteria:** Mild-to-moderate CTS based on clinical criteria and electrodiagnostic tests
Interventions	Group 1: splint + MEX Group 2: splint + ultrasound Group 3: MEX alone Group 4: ultrasound alone Commercially available hand splint was used to keep the wrist in the neutral position. Participants who received the hand splint were advised to use the splint during sleep.
Outcomes	Outcomes evaluated at baseline and at 7, 12 and 52 weeks follow-up

Soon 2015 *(Continued)*

	1. BCTQ 2. 6-point global rating of change scale (GROC, 1 = much worse, 2 =worse, 3 = no change, 4 = improved, 5 = much improved, 6 = completely recovered) 3. Electrodiagnostic test 4. 36-item Short Form Health Survey (SF-36) 5. Grip and tip-pinch strength using a digital dynamometer
Notes	Report available only as a conference abstract

BCTQ: Boston Carpal Tunnel Questionnaire
CTS: carpal tunnel syndrome
DML: distal motor latency
EMG: electromyography
GROC: Global Rating of Change
MEX: multimodal approach comprising of manual mobilisation techniques, education and nerve and tendon gliding exercises
NCV: nerve conduction velocity
RCT: randomised controlled trial
SF-36: 36-Item Short Form Health Survey
SNCV: sensory nerve conduction velocity
VAS: visual analog scale

Characteristics of ongoing studies *[ordered by study ID]*

Atroshi 2019

Study name	Evaluation of wrist splinting for the treatment of carpal tunnel syndrome
Methods	Study design: Prospective, randomised, parallel-group superiority clinical trial Setting: Department of Orthopedics, Hässleholm-Kristianstad-Ystad
Participants	**Details of sampling frame:** Total n for randomisation = 112 **Gender distribution:** **Age:** 25 to 65 years old **Duration of CTS symptoms:** **Inclusion criteria** 1. Primary, idiopathic CTS 2. Age 25–65 years, either sex 3. Symptoms of classic or probable CTS according to the criteria in the Katz hand diagram 4. Two surgeons (specialists in orthopaedic or hand surgery) independently diagnose the participant's CTS 5. Symptom duration of at least 1 month **Exclusion criteria** 1. CTS classified as severe (thenar muscle atrophy or 2-point discrimination exceeding 8 mm in at least one finger) 2. Treatment of the study hand with a wrist splint in the past 12 months 3. Previous steroid injection for CTS in the study hand 4. Inflammatory joint disease

Atroshi 2019 *(Continued)*

	5. Vibration-induced neuropathy 6. Polyneuropathy 7. Current pregnancy 8. Trauma to the study hand in the past 12 months 9. Previous CTS surgery in the study hand 10.Inability to complete questionnaires because of language difficulties or cognitive disorder 11.Severe medical illness 12.Known abuse of drugs or alcohol or both
Interventions	Group 1: rigid wrist splint Group 2: soft wrist bandage (placebo) Splints and soft wrist bandages are going to be used initially for 6 weeks at night and, if possible, during the day
Outcomes	Outcomes will be measured at baseline and at 6, 12, 24, and 52 weeks after treatment starts. 1. 6-item CTS symptoms scale 2. 11-item Disabilities of the Arm, Shoulder, and Hand (QuickDASH) scale 3. EuroQol 5-dimension (EQ-5D) health status and quality of life measure 4. Physical examination (grip strength and pinch strength) 5. Nerve conduction tests 6. Measurement of actual splint and bandage use 7. Referral to surgery
Starting date	Recruitment started 4 June 2018 and was expected to conclude by the end of 2020.
Contact information	Correspondence: Isam Atroshi, isam.atroshi@med.lu.se 1. Department of Clinical Sciences – Orthopedics, Lund University, SE-22100 Lund, Sweden 2. Department of Orthopedics Hässleholm-Kristianstad, Hässleholm Hospital, SE-28125 Hässleholm, Sweden
Notes	

IRCT20120716010297N5

Study name	The long-term effect of low level laser therapy on clinical symptoms and electrophysiologic parameters in patients with carpal tunnel syndrome
Methods	Study design: Double-blind, RCT Setting: outpatient clinics of Isfahan University of Medical Sciences
Participants	**Details of sampling frame:** Target sample size = 64 **Gender:** Both **Age:** From 30 years old to 65 years old

IRCT20120716010297N5 *(Continued)*

	Inclusion criteria: 1. Pain and numbness in the median nerve area 2. Positive clinical CTS tests 3. Mild or moderate CTS **Exclusion criteria:** 1. Severe CTS 2. Those receiving analgesic or anti-inflammatory drugs 3. History of steroid injection for CTS 4. History of diabetes or peripheral neuropathy
Interventions	Group 1: low level laser therapy Group 2: sham laser therapy + vitamin B_1 (300 mg per day) + static night splinting for wrist for 2 months
Outcomes	Outcomes measured at baseline and 6 months after treatment 1. Pain (VAS) 2. Nerve conduction (methods of measurement "Functional Severity Score, Symptoms Severity Scores" [as stated]) 3. Peak sensory latency 4. DML
Starting date	2014/06/05
Contact information	Shila Haghighat, +98 31 3233 0091, sh-haghighat@med.mui.ac.ir
Notes	Recruitment status: not yet recruiting

IRCT20200219046552N1

Study name	Comparison of local corticosteroid injection and high-intensity laser outcomes in moderate carpal tunnel syndrome (CTS)
Methods	Study design: A concealed, randomised, open-label, sham-controlled clinical trial with a parallel-group design
Participants	**Details of sampling frame:** Target sample size: 126 **Gender:** Both **Age:** No age limit **Inclusion criteria**: 1. Patients with unilateral or bilateral CTS according to median nerve electrophysiology (EMG-NCV) studies **Exclusion criteria:**

IRCT20200219046552N1 *(Continued)*

	1. History of wrist surgery 2. Polyneuropathy 3. Brachial plexopathy or thoracic outlet syndrome 4. History of thrombocytopenia 5. Platelet disorder 6. Systemic infection 7. Pregnancy 8. Rheumatologic disorders 9. Previous injection of cortisone for treatment of CTS 10.Thenar muscle atrophy
Interventions	Group 1: splint + painkillers (meloxicam 15 mg) + vitamin B_1 Group 2: 40 mg of methylprednisolone (Depromedrol) in combination with 1% lidocaine Group 3: laser therapy
Outcomes	Outcomes evaluated at baseline and 6 months later. 1. BCTQ Symptom Severity Scale 2. BCTQ Functional Status Scale 3. Pain (VAS) 4. Distal sensory latency 5. Distal motor latency 6. Medical complications
Starting date	20 April 2020
Contact information	Mozaffar Hosseininezhad, +98 13 3332 2444, hosseininezhadm@gmail.com
Notes	Recruitment status: recruiting

JPRN-UMIN000017952

Study name	Nerve gliding exercise for carpal tunnel syndrome
Methods	Study design: Interventional, factorial, randomised, open (no blinding)
Participants	**Details of sampling frame:** Sample size: 60 **Gender:** Both **Age:** 20 to 65 years old **Inclusion criteria:** Grade 1 (Hamada classification) **Exclusion criteria:** 1. Diabetes mellitus

JPRN-UMIN000017952 *(Continued)*	2. Malignancy 3. Pregnancy etc.
Interventions	Group 1: nerve gliding, splinting, rest Group 2: splinting, rest Group 3: rest
Outcomes	Improvement of symptoms
Starting date	15 June 2015
Contact information	Yuki Hara, 029-8533219, yukihara@md.tsukuba.ac.jp
Notes	Recruitment status: recruiting

NCT04017390	
Study name	The effect of theraworx foam on the cross-sectional area of the median nerve in patients with CTS
Methods	Study design: Randomised, parallel assignment, double (participant, investigator) masked
Participants	**Details of sampling frame:** Estimated enrolment = 60 participants **Age:** 18 years and older **Inclusion criteria** 1. Diagnosis of CTS 2. Age 18 years or older 3. Interest in non-surgical treatment of CTS **Exclusion criteria** 1. Prior carpal tunnel release 2. Non-English speaking 3. Skin lesions/rashes on hand being treated 4. Current use of topical anti-inflammatory medication 5. Other diagnoses that would impact results (determined by principal investigator)
Interventions	Group 1: Theraworx foam Group 2: placebo foam Group 3: Theraworx foam and night splint Group 4: placebo foam and night-time splint
Outcomes	Outcomes evaluated at baseline and after treatment (2 weeks) 1. Improvement (decrease) in size of median nerve at the wrist 2. BCTQ symptom and function

NCT04017390 *(Continued)*

	3. CTS-6 score 4. Disabilities of the Arm, Shoulder, and Hand score
Starting date	Estimated study start date: December 2021
Contact information	1. John Fowler, 412-605-3245, fowlerjr@upmc.edu 2. Karen Wasil, 412-605-3221, wasilkf2[at]upmc.edu
Notes	

NCT04515966

Study name	Randomised controlled trial of ultrasound-guided steroid injection versus wrist splint in patients with CTS
Methods	Study design: Randomised, parallel assignment, open-label (no masking)
Participants	**Details of sampling frame:** Estimated enrolment: 70 participants **Gender:** Both **Age:** 18 years to 75 years (adult, older adult) **Duration of CTS symptoms:** **Inclusion criteria** 1. People with typical symptoms of CTS, including nocturnal, postural, or usage-associated paraesthesia of the hand 2. Symptoms persisting for at least 3 months before the study 3. Patients with mild-to-moderate symptoms 4. No history of steroid injections in the past 5. No history of carpal tunnel release surgery 6. Age 18 to 75 years **Exclusion criteria** 1. Thenar atrophy or muscle weakness 2. Severe CTS 3. Pregnancy 4. Hypothyroidism 5. Diabetes mellitus 6. Chronic renal failure 7. Rheumatoid arthritis 8. Orthopaedic or neurological disorders that could mimic CTS such as cervical radiculopathy, polyneuropathy, proximal median nerve entrapment, or thoracic outlet syndrome 9. History of distal radius fracture 10. Anticoagulation 11. Chronic use of systemic corticosteroids

NCT04515966 *(Continued)*

	12.Known allergy to corticosteroids and local anaesthetics
Interventions	Group 1: ultrasound-guided steroid injection Group 2: wrist splint
Outcomes	Outcomes evaluated at baseline and after treatment (6 weeks, 12 weeks, 6 months, 1 year). 1. BCTQ Symptom Severity Scale 2. BCTQ Functional Status Scale 3. VAS 4. Change in median nerve dimensions
Starting date	Estimated study start date: 1 October 2020
Contact information	Roy N Morcos, (330)729-8700, roy_morcos@mercy.com
Notes	

NCT04993703

Study name	Effect of kinesiotaping and night splinting in patients with carpal tunnel syndrome
Methods	Study design: Double-blind (participant-, outcomes assessor-blinded) RCT
Participants	**Details of sampling frame:** Estimated enrolment: 45 participants **Gender:** Both **Age:** Ages eligible for study: 30 years to 60 years **Inclusion criteria:** 1. This study included people with moderate CTS, confirmed by electroneurographic examination 2. "Did not recruit any treatment (including physiotherapy or surgical release)" [as stated] **Exclusion criteria:** 1. People with thenar muscle atrophy 2. People with mild CTS
Interventions	Group 1: kinesiotaping Group 2: night splinting Group 3: control group
Outcomes	Outcomes assessed at baseline and 8-week follow-up 1. Functional impairment (BCTQ, 1-5 scale, higher is worse) 2. Pain intensity (VAS at rest, activity and at night, 0-100 scale, higher is worse) 3. Paraesthesia (VAS at rest, activity and at night, 0-100 scale, higher is worse)

NCT04993703 *(Continued)*

Starting date	2021/08/06
Contact information	Leyla Eraslan, +905348488373, leylaeraslan@hacettepe.edu.tr
Notes	Recruitment status: recruiting

BCTQ: Boston Carpal Tunnel Questionnaire
CTS: carpal tunnel syndrome
DML: distal motor latency
EMG: electromyography
EQ-5D: EuroQol 5-dimension health status and quality of life measure
NCV: nerve conduction velocity
quickDASH: 11-item Disabilities of the Arm, Shoulder, and Hand scale
RCT: randomised controlled trial
VAS: visual analog scale

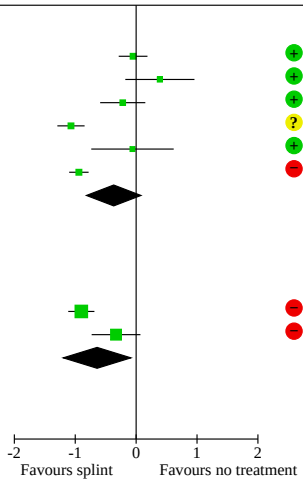
DATA AND ANALYSES

Comparison 1. SPLINT VERSUS NO ACTIVE TREATMENT

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 CTS symptoms (BCTQ)	7		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1.1 Short-term improvement: 3 months or less	6	306	Mean Difference (IV, Random, 95% CI)	-0.37 [-0.82, 0.08]
1.1.2 Long-term improvement: > 3months	2	144	Mean Difference (IV, Random, 95% CI)	-0.64 [-1.20, -0.08]
1.2 Function (BCTQ)	6		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.2.1 Short-term improvement: 3 months or less	6	306	Mean Difference (IV, Random, 95% CI)	-0.24 [-0.44, -0.03]
1.2.2 Long-term improvement: > 3 months	1	34	Mean Difference (IV, Random, 95% CI)	-0.25 [-0.68, 0.18]
1.3 Overall improvement	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.3.1 Short-term improvement: 3 months or less	1	80	Risk Ratio (M-H, Fixed, 95% CI)	3.86 [2.29, 6.51]
1.4 Adverse effects	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.4.1 Adverse effects	1	80	Risk Ratio (M-H, Random, 95% CI)	15.00 [0.89, 254.13]
1.5 Referral for surgery	3	243	Risk Ratio (M-H, Random, 95% CI)	0.47 [0.14, 1.58]

Analysis 1.1. Comparison 1: SPLINT VERSUS NO ACTIVE TREATMENT, Outcome 1: CTS symptoms (BCTQ)

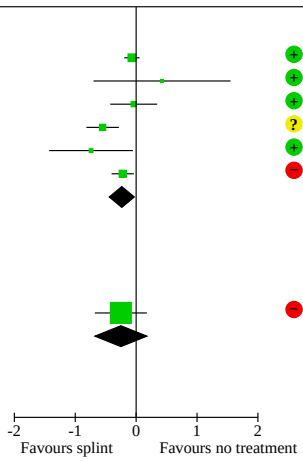
Study or Subgroup	Splint Mean	SD	Total	No treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F
1.1.1 Short-term improvement: 3 months or less									
Boonhong 2017	1.27	0.41	28	1.32	0.47	26	18.2%	-0.05 [-0.29 , 0.19]	+ + − − ? +
Geler Kulcu 2016	2.61	1.07	20	2.22	0.73	20	14.6%	0.39 [-0.18 , 0.96]	+ + − − ? ?
Hall 2013	2.38	0.77	30	2.6	0.62	24	16.9%	-0.22 [-0.59 , 0.15]	+ ? − − ? +
Manente 2001	1.54	0.4	40	2.61	0.6	40	18.3%	-1.07 [-1.29 , -0.85]	? ? − − + −
Oncu 2014	2.99	0.98	15	3.05	0.91	15	13.3%	-0.06 [-0.74 , 0.62]	+ + − − ? −
Premoselli 2006	1.63	0.25	24	2.57	0.31	24	18.7%	-0.94 [-1.10 , -0.78]	− − − − + +
Subtotal (95% CI)			**157**			**149**	**100.0%**	**-0.37 [-0.82 , 0.08]**	
Heterogeneity: Tau² = 0.27; Chi² = 72.02, df = 5 (P < 0.00001); I² = 93%									
Test for overall effect: Z = 1.61 (P = 0.11)									
1.1.2 Long-term improvement: > 3months									
Premoselli 2006	1.48	0.19	18	2.38	0.4	16	54.6%	-0.90 [-1.11 , -0.69]	− − − − + +
Werner 2005	2.19	1.06	63	2.52	1.06	47	45.4%	-0.33 [-0.73 , 0.07]	− − − − ? +
Subtotal (95% CI)			**81**			**63**	**100.0%**	**-0.64 [-1.20 , -0.08]**	
Heterogeneity: Tau² = 0.14; Chi² = 6.05, df = 1 (P = 0.01); I² = 83%									
Test for overall effect: Z = 2.26 (P = 0.02)									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 1.2. Comparison 1: SPLINT VERSUS NO ACTIVE TREATMENT, Outcome 2: Function (BCTQ)

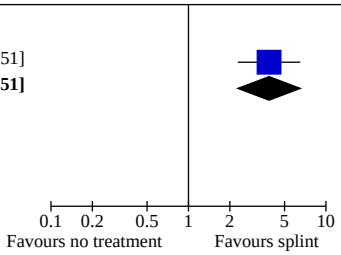
Study or Subgroup	Splint Mean	SD	Total	No treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F
1.2.1 Short-term improvement: 3 months or less									
Boonhong 2017	1.06	0.281	28	1.13	0.185	26	28.5%	-0.07 [-0.20 , 0.06]	+ + − − ? +
Geler Kulcu 2016	2.463	2.463	20	2.038	0.725	20	3.0%	0.43 [-0.70 , 1.55]	+ + − − ? ?
Hall 2013	2.04	0.74	30	2.08	0.7	24	15.1%	-0.04 [-0.43 , 0.35]	+ ? − − ? +
Manente 2001	1.48	0.5	40	2.03	0.7	40	20.8%	-0.55 [-0.82 , -0.28]	? ? − − + −
Oncu 2014	2.23	1.12	15	2.97	0.77	15	7.0%	-0.74 [-1.43 , -0.05]	+ + − − ? −
Premoselli 2006	1.74	0.37	24	1.96	0.27	24	25.5%	-0.22 [-0.40 , -0.04]	− − − − + +
Subtotal (95% CI)			**157**			**149**	**100.0%**	**-0.24 [-0.44 , -0.03]**	
Heterogeneity: Tau² = 0.03; Chi² = 14.65, df = 5 (P = 0.01); I² = 66%									
Test for overall effect: Z = 2.24 (P = 0.03)									
1.2.2 Long-term improvement: > 3 months									
Premoselli 2006	1.52	0.39	18	1.77	0.79	16	100.0%	-0.25 [-0.68 , 0.18]	− − − − + +
Subtotal (95% CI)			**18**			**16**	**100.0%**	**-0.25 [-0.68 , 0.18]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.15 (P = 0.25)									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 1.3. Comparison 1: SPLINT VERSUS NO ACTIVE TREATMENT, Outcome 3: Overall improvement

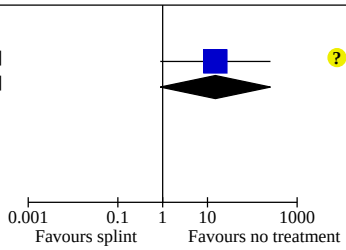
Study or Subgroup	Splint Events	Splint Total	No treatment Events	No treatment Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F
1.3.1 Short-term improvement: 3 months or less							
Manente 2001	40	40	10	40	100.0%	3.86 [2.29 , 6.51]	? ? − − + −
Subtotal (95% CI)		**40**		**40**	**100.0%**	**3.86 [2.29 , 6.51]**	
Total events:	40		10				
Heterogeneity: Not applicable							
Test for overall effect: Z = 5.06 (P < 0.00001)							



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 1.4. Comparison 1: SPLINT VERSUS NO ACTIVE TREATMENT, Outcome 4: Adverse effects

Study or Subgroup	Splint Events	Splint Total	No treatment Events	No treatment Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F
1.4.1 Adverse effects							
Manente 2001	7	40	0	40	100.0%	15.00 [0.89 , 254.13]	? ? − − + −
Subtotal (95% CI)		**40**		**40**	**100.0%**	**15.00 [0.89 , 254.13]**	
Total events:	7		0				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.88 (P = 0.06)							

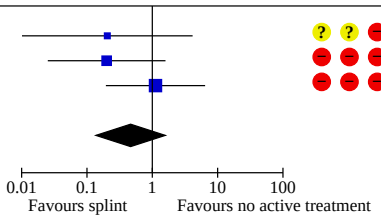


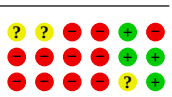
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 1.5. Comparison 1: SPLINT VERSUS NO ACTIVE TREATMENT, Outcome 5: Referral for surgery

Study or Subgroup	Splint Events	Splint Total	No active treatment Events	No active treatment Total	Weight	Risk Ratio M-H, Random, 95% CI
Manente 2001	0	41	2	42	16.5%	0.20 [0.01 , 4.14]
Premoselli 2006	1	25	5	25	34.7%	0.20 [0.03 , 1.59]
Werner 2005	3	63	2	47	48.8%	1.12 [0.19 , 6.43]
Total (95% CI)		**129**		**114**	**100.0%**	**0.47 [0.14 , 1.58]**
Total events:	4		9			

Heterogeneity: Tau² = 0.00; Chi² = 1.92, df = 2 (P = 0.38); I² = 0%
Test for overall effect: Z = 1.23 (P = 0.22)
Test for subgroup differences: Not applicable





Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

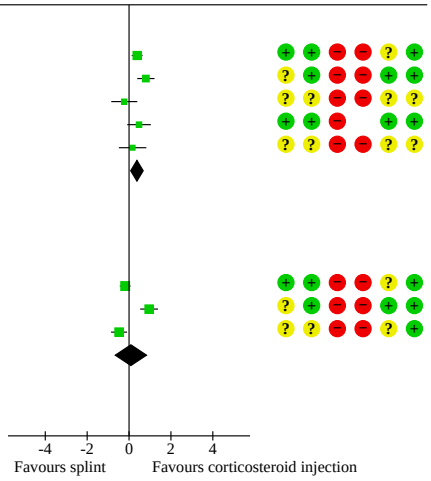
Comparison 2. SPLINT VERSUS CORTICOSTEROID INJECTION

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 CTS symptoms	6		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1.1 Short-term improvement: 3 months or less	5	459	Std. Mean Difference (IV, Random, 95% CI)	0.38 [0.08, 0.68]
2.1.2 Long-term improvement: over 3 months	3	437	Std. Mean Difference (IV, Random, 95% CI)	0.09 [-0.66, 0.83]
2.2 Function (BCTQ)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.2.1 Short-term improvement: 3 months or less	5	459	Mean Difference (IV, Random, 95% CI)	0.16 [-0.04, 0.36]
2.2.2 Long-term improvement: over 3 months	2	329	Mean Difference (IV, Random, 95% CI)	0.33 [-0.40, 1.06]
2.3 Overall improvement	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.3.1 Short-term improvement: 3 months or less	1	99	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.39, 0.84]
2.3.2 Long-term improvement: over 3 months	1	95	Risk Ratio (M-H, Random, 95% CI)	0.36 [0.22, 0.58]
2.4 Health-related quality of life	2		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.4.1 Short-term improvement: 3 months or less	2	270	Std. Mean Difference (IV, Random, 95% CI)	-0.25 [-0.77, 0.27]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.4.2 Long-term improvement: over 3 months	1	234	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-0.21, 0.30]
2.5 Adverse effects	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.5.1 Adverse effects	6	590	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.08, 1.26]
2.6 Referral for surgery	2	334	Risk Ratio (M-H, Random, 95% CI)	0.60 [0.33, 1.09]

Analysis 2.1. Comparison 2: SPLINT VERSUS CORTICOSTEROID INJECTION, Outcome 1: CTS symptoms

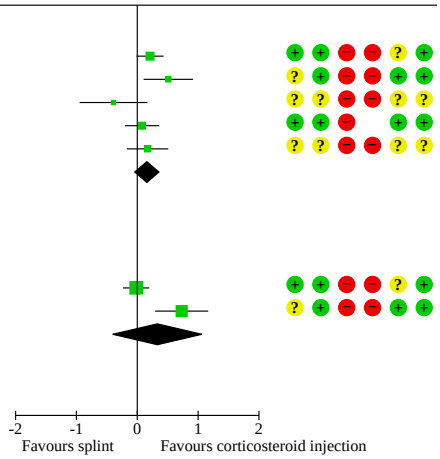
Study or Subgroup	Splint Mean	Splint SD	Splint Total	Corticosteroid injection Mean	Corticosteroid injection SD	Corticosteroid injection Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.1.1 Short-term improvement: 3 months or less								
Chesterton 2018	2.43	0.76	118	2.12	0.84	116	31.5%	0.39 [0.13 , 0.64]
De Moraes 2021	2.55	0.95	47	1.78	0.95	52	23.2%	0.80 [0.39 , 1.21]
Kocaoglu 2017	1.32	0.96	20	1.59	1.33	20	14.8%	-0.23 [-0.85 , 0.39]
So 2018	1.81	0.45	25	1.58	0.5	25	16.7%	0.48 [-0.09 , 1.04]
Taspinar 2007	1.5	0.38	18	1.42	0.53	18	13.8%	0.17 [-0.49 , 0.82]
Subtotal (95% CI)			**228**			**231**	**100.0%**	**0.38 [0.08 , 0.68]**
Heterogeneity: Tau² = 0.06; Chi² = 8.19, df = 4 (P = 0.08); I² = 51%								
Test for overall effect: Z = 2.47 (P = 0.01)								
2.1.2 Long-term improvement: over 3 months								
Chesterton 2018	2.18	0.75	118	2.33	0.86	116	34.7%	-0.19 [-0.44 , 0.07]
De Moraes 2021	2.73	0.98	45	1.83	0.89	50	32.3%	0.96 [0.53 , 1.38]
Sevim 2004	13.04	5.01	51	15.79	6.32	57	33.0%	-0.48 [-0.86 , -0.09]
Subtotal (95% CI)			**214**			**223**	**100.0%**	**0.09 [-0.66 , 0.83]**
Heterogeneity: Tau² = 0.40; Chi² = 27.19, df = 2 (P < 0.00001); I² = 93%								
Test for overall effect: Z = 0.23 (P = 0.82)								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 2.2. Comparison 2: SPLINT VERSUS CORTICOSTEROID INJECTION, Outcome 2: Function (BCTQ)

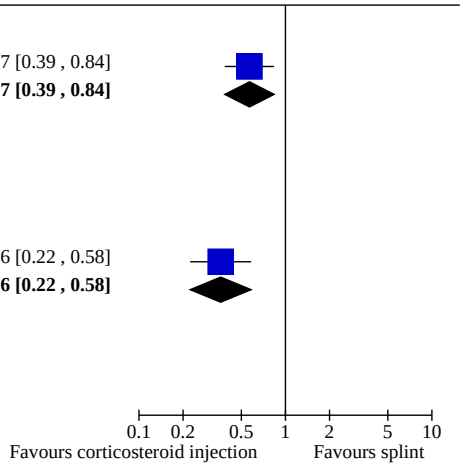
Study or Subgroup	Splint Mean	Splint SD	Splint Total	Corticosteroid injection Mean	Corticosteroid injection SD	Corticosteroid injection Total	Weight	Mean Difference IV, Random, 95% CI
2.2.1 Short-term improvement: 3 months or less								
Chesterton 2018	2.09	0.86	118	1.88	0.88	116	29.7%	0.21 [-0.01 , 0.43]
De Moraes 2021	2.41	1.07	47	1.9	0.98	52	16.0%	0.51 [0.10 , 0.92]
Kocaoglu 2017	1.15	0.81	20	1.54	0.98	20	10.0%	-0.39 [-0.95 , 0.17]
So 2018	1.46	0.46	25	1.38	0.55	25	24.4%	0.08 [-0.20 , 0.36]
Taspinar 2007	1.58	0.54	18	1.41	0.5	18	19.9%	0.17 [-0.17 , 0.51]
Subtotal (95% CI)			**228**			**231**	**100.0%**	**0.16 [-0.04 , 0.36]**
Heterogeneity: Tau² = 0.02; Chi² = 7.10, df = 4 (P = 0.13); I² = 44%								
Test for overall effect: Z = 1.56 (P = 0.12)								
2.2.2 Long-term improvement: over 3 months								
Chesterton 2018	1.89	0.84	118	1.91	0.84	116	53.3%	-0.02 [-0.24 , 0.20]
De Moraes 2021	2.64	1.12	45	1.91	1.04	50	46.7%	0.73 [0.29 , 1.17]
Subtotal (95% CI)			**163**			**166**	**100.0%**	**0.33 [-0.40 , 1.06]**
Heterogeneity: Tau² = 0.25; Chi² = 9.14, df = 1 (P = 0.003); I² = 89%								
Test for overall effect: Z = 0.88 (P = 0.38)								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

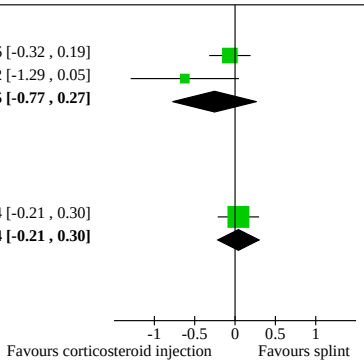
Analysis 2.3. Comparison 2: SPLINT VERSUS CORTICOSTEROID INJECTION, Outcome 3: Overall improvement

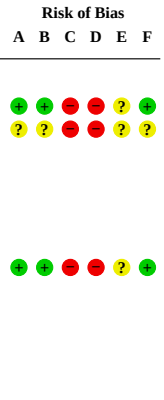
Study or Subgroup	Splint Events	Splint Total	Corticosteroid injection Events	Corticosteroid injection Total	Weight	Risk Ratio M-H, Random, 95% CI
2.3.1 Short-term improvement: 3 months or less						
De Moraes 2021	19	47	37	52	100.0%	0.57 [0.39 , 0.84]
Subtotal (95% CI)		**47**		**52**	**100.0%**	**0.57 [0.39 , 0.84]**
Total events:	19		37			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.86 (P = 0.004)						
2.3.2 Long-term improvement: over 3 months						
De Moraes 2021	13	45	40	50	100.0%	0.36 [0.22 , 0.58]
Subtotal (95% CI)		**45**		**50**	**100.0%**	**0.36 [0.22 , 0.58]**
Total events:	13		40			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.17 (P < 0.0001)						



Analysis 2.4. Comparison 2: SPLINT VERSUS CORTICOSTEROID INJECTION, Outcome 4: Health-related quality of life

Study or Subgroup	Splint Mean	Splint SD	Splint Total	Corticosteroid injection Mean	Corticosteroid injection SD	Corticosteroid injection Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.4.1 Short-term improvement: 3 months or less								
Chesterton 2018	0.781	0.205	118	0.794	0.2	116	66.0%	-0.06 [-0.32 , 0.19]
Taspinar 2007	-0.66	0.41	18	-0.42	0.34	18	34.0%	-0.62 [-1.29 , 0.05]
Subtotal (95% CI)			**136**			**134**	**100.0%**	**-0.25 [-0.77 , 0.27]**
Heterogeneity: Tau² = 0.09; Chi² = 2.33, df = 1 (P = 0.13); I² = 57%								
Test for overall effect: Z = 0.96 (P = 0.34)								
2.4.2 Long-term improvement: over 3 months								
Chesterton 2018	0.826	0.174	118	0.819	0.161	116	100.0%	0.04 [-0.21 , 0.30]
Subtotal (95% CI)			**118**			**116**	**100.0%**	**0.04 [-0.21 , 0.30]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.32 (P = 0.75)								

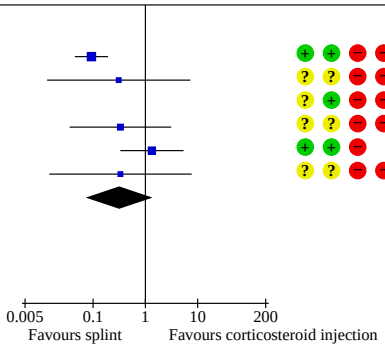


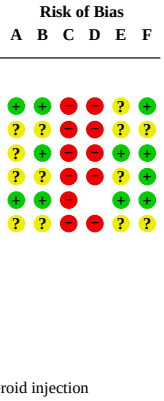


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 2.5. Comparison 2: SPLINT VERSUS CORTICOSTEROID INJECTION, Outcome 5: Adverse effects

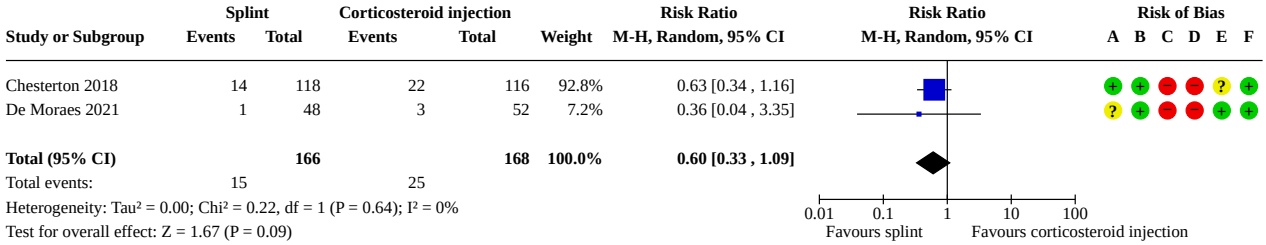
Study or Subgroup	Splint Events	Splint Total	Corticosteroid injection Events	Corticosteroid injection Total	Weight	Risk Ratio M-H, Random, 95% CI
2.5.1 Adverse effects						
Chesterton 2018	7	118	74	116	31.4%	0.09 [0.04 , 0.19]
De Entrambasaguas 2006	0	26	1	24	12.4%	0.31 [0.01 , 7.23]
De Moraes 2021	0	48	0	52		Not estimable
Sevim 2004	1	60	3	60	18.2%	0.33 [0.04 , 3.11]
So 2018	4	25	3	25	25.6%	1.33 [0.33 , 5.36]
Taspinar 2007	0	18	1	18	12.5%	0.33 [0.01 , 7.68]
Subtotal (95% CI)		**295**		**295**	**100.0%**	**0.32 [0.08 , 1.26]**
Total events:	12		82			
Heterogeneity: Tau² = 1.46; Chi² = 11.95, df = 4 (P = 0.02); I² = 67%						
Test for overall effect: Z = 1.63 (P = 0.10)						





Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 2.6. Comparison 2: SPLINT VERSUS CORTICOSTEROID INJECTION, Outcome 6: Referral for surgery



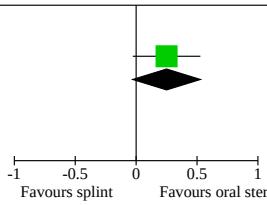
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Comparison 3. SPLINT VERSUS ORAL STEROID

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 CTS symptoms (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1.1 Short-term improvement: 3 months or less	1	71	Mean Difference (IV, Random, 95% CI)	0.25 [-0.03, 0.53]
3.2 Function (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.2.1 Short-term improvement: 3 months or less	1	71	Mean Difference (IV, Random, 95% CI)	0.12 [-0.06, 0.30]
3.3 Adverse effects	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.3.1 Adverse effects	1	71	Risk Ratio (M-H, Random, 95% CI)	4.86 [0.24, 97.86]

Analysis 3.1. Comparison 3: SPLINT VERSUS ORAL STEROID, Outcome 1: CTS symptoms (BCTQ)

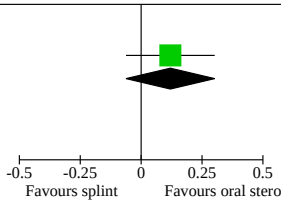
Study or Subgroup	Splint Mean	Splint SD	Splint Total	Oral steroid Mean	Oral steroid SD	Oral steroid Total	Weight	Mean Difference IV, Random, 95% CI
3.1.1 Short-term improvement: 3 months or less								
Mishra 2006	2.43	0.56	36	2.18	0.63	35	100.0%	0.25 [-0.03 , 0.53]
Subtotal (95% CI)			**36**			**35**	**100.0%**	**0.25 [-0.03 , 0.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.77 (P = 0.08)								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 3.2. Comparison 3: SPLINT VERSUS ORAL STEROID, Outcome 2: Function (BCTQ)

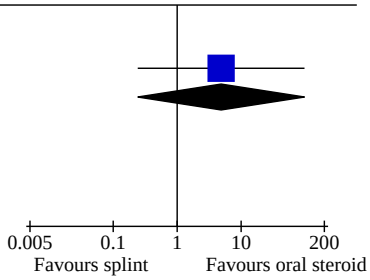
Study or Subgroup	Splint Mean	Splint SD	Splint Total	Oral steroid Mean	Oral steroid SD	Oral steroid Total	Weight	Mean Difference IV, Random, 95% CI
3.2.1 Short-term improvement: 3 months or less								
Mishra 2006	1.57	0.43	36	1.45	0.35	35	100.0%	0.12 [-0.06 , 0.30]
Subtotal (95% CI)			**36**			**35**	**100.0%**	**0.12 [-0.06 , 0.30]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.29 (P = 0.20)								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 3.3. Comparison 3: SPLINT VERSUS ORAL STEROID, Outcome 3: Adverse effects

Study or Subgroup	Splint Events	Splint Total	Oral steroid Events	Oral steroid Total	Weight	Risk Ratio M-H, Random, 95% CI
3.3.1 Adverse effects						
Mishra 2006	2	36	0	35	100.0%	4.86 [0.24 , 97.86]
Subtotal (95% CI)		**36**		**35**	**100.0%**	**4.86 [0.24 , 97.86]**
Total events:	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.03 (P = 0.30)						



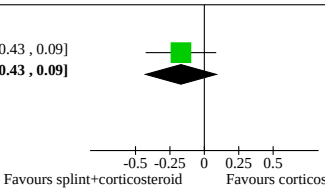
Comparison 4. SPLINT PLUS CORTICOSTEROID INJECTION VERSUS CORTICOSTEROID INJECTION

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 CTS symptoms (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1.1 Short-term improvement: 3 months or less	1	52	Mean Difference (IV, Random, 95% CI)	-0.17 [-0.43, 0.09]
4.2 Function (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.2.1 Short-term improvement: 3 months or less	1	52	Mean Difference (IV, Random, 95% CI)	-0.05 [-0.28, 0.18]
4.3 Overall improvement	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.3.1 Short-term improvement: 3 months or less	1	52	Risk Ratio (M-H, Random, 95% CI)	1.33 [0.90, 1.97]

Analysis 4.1. Comparison 4: SPLINT PLUS CORTICOSTEROID INJECTION VERSUS CORTICOSTEROID INJECTION, Outcome 1: CTS symptoms (BCTQ)

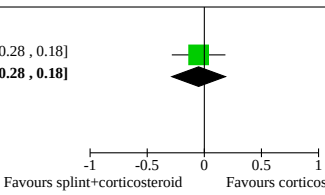
Study or Subgroup	Splint plus corticosteroid injection Mean	SD	Total	Corticosteroid injection Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
4.1.1 Short-term improvement: 3 months or less								
Wang 2017	1.32	0.43	26	1.49	0.51	26	100.0%	-0.17 [-0.43 , 0.09]
Subtotal (95% CI)			**26**			**26**	**100.0%**	**-0.17 [-0.43 , 0.09]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.30 (P = 0.19)								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 4.2. Comparison 4: SPLINT PLUS CORTICOSTEROID INJECTION VERSUS CORTICOSTEROID INJECTION, Outcome 2: Function (BCTQ)

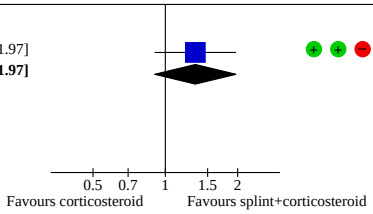
Study or Subgroup	Splint plus corticosteroid injection Mean	SD	Total	Corticosteroid injection Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
4.2.1 Short-term improvement: 3 months or less								
Wang 2017	1.27	0.5	26	1.32	0.35	26	100.0%	-0.05 [-0.28 , 0.18]
Subtotal (95% CI)			**26**			**26**	**100.0%**	**-0.05 [-0.28 , 0.18]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.42 (P = 0.68)								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 4.3. Comparison 4: SPLINT PLUS CORTICOSTEROID INJECTION VERSUS CORTICOSTEROID INJECTION, Outcome 3: Overall improvement

Study or Subgroup	Splint plus corticosteroid injection Events	Total	Corticosteroid injection Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
4.3.1 Short-term improvement: 3 months or less						
Wang 2017	20	26	15	26	100.0%	1.33 [0.90 , 1.97]
Subtotal (95% CI)		**26**		**26**	**100.0%**	**1.33 [0.90 , 1.97]**
Total events:	20		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.44 (P = 0.15)						



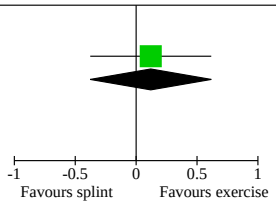
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Comparison 5. SPLINT VERSUS EXERCISE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 CTS symptoms (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1.1 Short-term improvement: 3 months or less	1	20	Mean Difference (IV, Random, 95% CI)	0.12 [-0.38, 0.62]
5.2 Function (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.2.1 Short-term improvement: 3 months or less	1	20	Mean Difference (IV, Random, 95% CI)	0.30 [-0.11, 0.71]

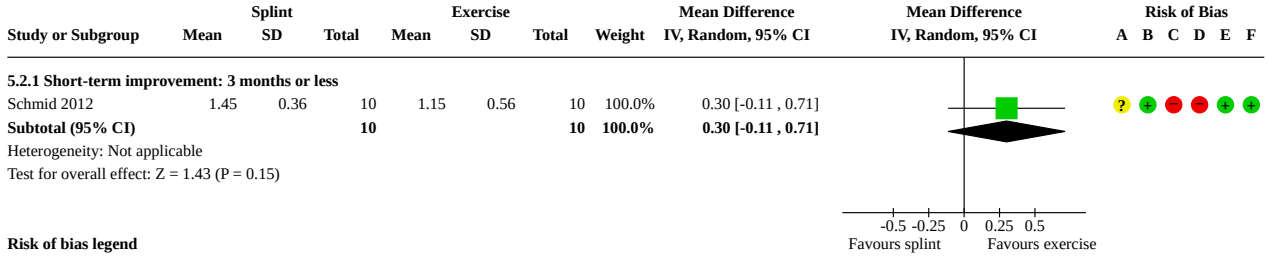
Analysis 5.1. Comparison 5: SPLINT VERSUS EXERCISE, Outcome 1: CTS symptoms (BCTQ)

Study or Subgroup	Splint Mean	SD	Total	Exercise Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
5.1.1 Short-term improvement: 3 months or less								
Schmid 2012	1.85	0.44	10	1.73	0.67	10	100.0%	0.12 [-0.38 , 0.62]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**0.12 [-0.38 , 0.62]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.47 (P = 0.64)								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 5.2. Comparison 5: SPLINT VERSUS EXERCISE, Outcome 2: Function (BCTQ)

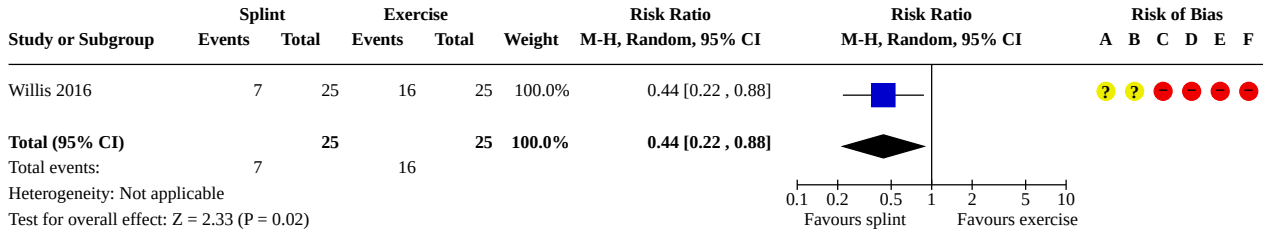


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Comparison 6. STRETCHING SPLINT VERSUS STRETCHING EXERCISES

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Referral for surgery	1	50	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.22, 0.88]

Analysis 6.1. Comparison 6: STRETCHING SPLINT VERSUS STRETCHING EXERCISES, Outcome 1: Referral for surgery



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Comparison 7. SPLINT VERSUS KINESIOLOGY TAPING

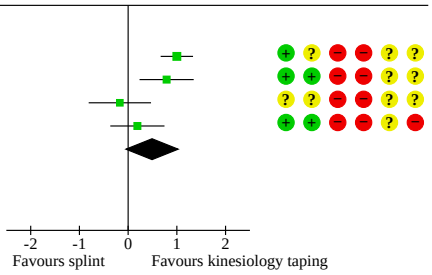
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 CTS symptoms (BCTQ)	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
7.1.1 Short-term improvement: 3 months or less	4	168	Mean Difference (IV, Random, 95% CI)	0.49 [-0.05, 1.03]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.2 Function (BCTQ)	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
7.2.1 Short-term improvement: 3 months or less	4	168	Mean Difference (IV, Random, 95% CI)	0.11 [-0.54, 0.75]

Analysis 7.1. Comparison 7: SPLINT VERSUS KINESIOLOGY TAPING, Outcome 1: CTS symptoms (BCTQ)

Study or Subgroup	Splint Mean	SD	Total	Kinesiology taping Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
7.1.1 Short-term improvement: 3 months or less								
Akturk 2018	3.27	0.42	30	2.27	0.8	28	29.1%	1.00 [0.67 , 1.33]
Geler Kulcu 2016	2.61	1.07	20	1.82	0.68	20	24.3%	0.79 [0.23 , 1.35]
Kocaoglu 2017	1.32	0.96	20	1.49	1.1	20	22.4%	-0.17 [-0.81 , 0.47]
Oncu 2014	2.86	0.83	15	2.67	0.72	15	24.2%	0.19 [-0.37 , 0.75]
Subtotal (95% CI)			**85**			**83**	**100.0%**	**0.49 [-0.05 , 1.03]**

Heterogeneity: Tau² = 0.23; Chi² = 13.44, df = 3 (P = 0.004); I² = 78%
Test for overall effect: Z = 1.79 (P = 0.07)



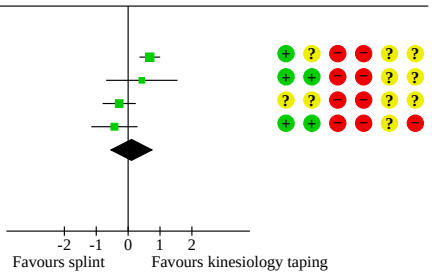
Risk of Bias: A B C D E F

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 7.2. Comparison 7: SPLINT VERSUS KINESIOLOGY TAPING, Outcome 2: Function (BCTQ)

Study or Subgroup	Splint Mean	SD	Total	Kinesiology taping Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
7.2.1 Short-term improvement: 3 months or less								
Akturk 2018	1.89	0.75	30	1.21	0.49	28	31.4%	0.68 [0.36 , 1.00]
Geler Kulcu 2016	2.46	2.46	20	2.03	0.68	20	16.8%	0.43 [-0.69 , 1.55]
Kocaoglu 2017	1.15	0.81	20	1.43	0.87	20	27.9%	-0.28 [-0.80 , 0.24]
Oncu 2014	2.23	1.12	15	2.66	0.89	15	23.8%	-0.43 [-1.15 , 0.29]
Subtotal (95% CI)			**85**			**83**	**100.0%**	**0.11 [-0.54 , 0.75]**

Heterogeneity: Tau² = 0.31; Chi² = 13.99, df = 3 (P = 0.003); I² = 79%
Test for overall effect: Z = 0.32 (P = 0.75)



Risk of Bias: A B C D E F

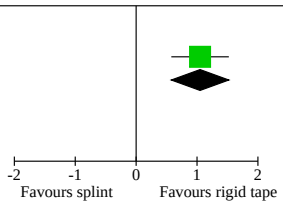
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Comparison 8. SPLINT VERSUS RIGID TAPE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 CTS symptoms (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
8.1.1 Short-term improvement: 3 months or less	1	30	Mean Difference (IV, Random, 95% CI)	1.05 [0.58, 1.52]
8.2 Function (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
8.2.1 Short-term improvement: 3 months or less	1	30	Mean Difference (IV, Random, 95% CI)	0.87 [0.48, 1.26]

Analysis 8.1. Comparison 8: SPLINT VERSUS RIGID TAPE, Outcome 1: CTS symptoms (BCTQ)

Study or Subgroup	Splint Mean	Splint SD	Splint Total	Rigid tape Mean	Rigid tape SD	Rigid tape Total	Weight	Mean Difference IV, Random, 95% CI
8.1.1 Short-term improvement: 3 months or less								
Eraslan 2014	2.53	0.8	15	1.48	0.48	15	100.0%	1.05 [0.58 , 1.52]
Subtotal (95% CI)			**15**			**15**	**100.0%**	**1.05 [0.58 , 1.52]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.36 (P < 0.0001)								

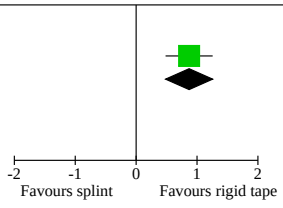


Risk of Bias: A B C D E F

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 8.2. Comparison 8: SPLINT VERSUS RIGID TAPE, Outcome 2: Function (BCTQ)

Study or Subgroup	Splint Mean	Splint SD	Splint Total	Rigid tape Mean	Rigid tape SD	Rigid tape Total	Weight	Mean Difference IV, Random, 95% CI
8.2.1 Short-term improvement: 3 months or less								
Eraslan 2014	2.58	0.61	15	1.71	0.46	15	100.0%	0.87 [0.48 , 1.26]
Subtotal (95% CI)			**15**			**15**	**100.0%**	**0.87 [0.48 , 1.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.41 (P < 0.0001)								



Risk of Bias: A B C D E F

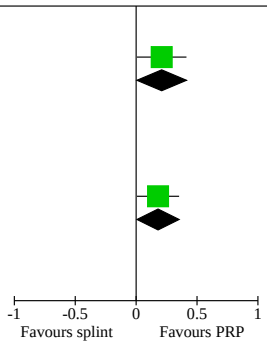
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Comparison 9. SPLINT VERSUS PLATELET RICH PLASMA (PRP)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.1 CTS symptoms (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
9.1.1 Short-term improvement: 3 months or less	1	60	Mean Difference (IV, Random, 95% CI)	0.21 [0.01, 0.41]
9.1.2 Long-term improvement: > 3 months	1	60	Mean Difference (IV, Random, 95% CI)	0.18 [0.01, 0.35]
9.2 Function (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
9.2.1 Short-term improvement: 3 months or less	1	60	Mean Difference (IV, Random, 95% CI)	0.35 [0.16, 0.54]
9.2.2 Long-term improvement: > 3 months	1	60	Mean Difference (IV, Random, 95% CI)	0.32 [0.12, 0.52]

Analysis 9.1. Comparison 9: SPLINT VERSUS PLATELET RICH PLASMA (PRP), Outcome 1: CTS symptoms (BCTQ)

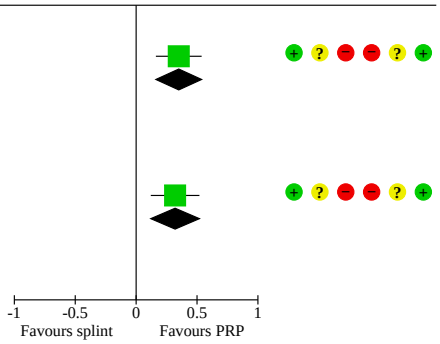
Study or Subgroup	Splint Mean	Splint SD	Splint Total	PRP Mean	PRP SD	PRP Total	Weight	Mean Difference IV, Random, 95% CI
9.1.1 Short-term improvement: 3 months or less								
Wu 2017	1.64	0.51	30	1.43	0.25	30	100.0%	0.21 [0.01 , 0.41]
Subtotal (95% CI)			**30**			**30**	**100.0%**	**0.21 [0.01 , 0.41]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.03 (P = 0.04)								
9.1.2 Long-term improvement: > 3 months								
Wu 2017	1.47	0.43	30	1.29	0.22	30	100.0%	0.18 [0.01 , 0.35]
Subtotal (95% CI)			**30**			**30**	**100.0%**	**0.18 [0.01 , 0.35]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.04 (P = 0.04)								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 9.2. Comparison 9: SPLINT VERSUS PLATELET RICH PLASMA (PRP), Outcome 2: Function (BCTQ)

Study or Subgroup	Splint Mean	Splint SD	Splint Total	PRP Mean	PRP SD	PRP Total	Weight	Mean Difference IV, Random, 95% CI
9.2.1 Short-term improvement: 3 months or less								
Wu 2017	1.7	0.45	30	1.35	0.27	30	100.0%	0.35 [0.16 , 0.54]
Subtotal (95% CI)			**30**			**30**	**100.0%**	**0.35 [0.16 , 0.54]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.65 (P = 0.0003)								
9.2.2 Long-term improvement: > 3 months								
Wu 2017	1.62	0.45	30	1.3	0.33	30	100.0%	0.32 [0.12 , 0.52]
Subtotal (95% CI)			**30**			**30**	**100.0%**	**0.32 [0.12 , 0.52]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.14 (P = 0.002)								



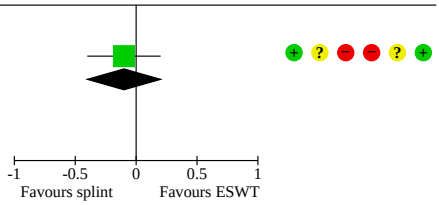
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Comparison 10. SPLINT VERSUS EXTRACORPOREAL SHOCK WAVE THERAPY (ESWT)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.1 CTS symptoms (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
10.1.1 Short-term improvement: 3 months or less	1	83	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.40, 0.20]
10.2 Function (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
10.2.1 Short-term improvement: 3 months or less	1	83	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.44, 0.24]

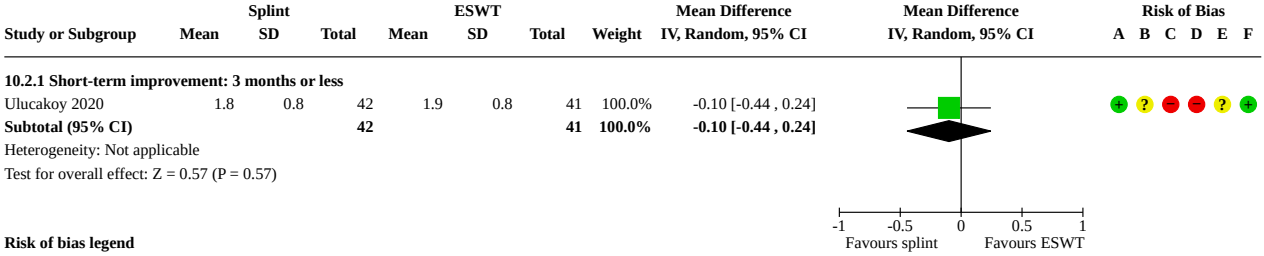
Analysis 10.1. Comparison 10: SPLINT VERSUS EXTRACORPOREAL SHOCK WAVE THERAPY (ESWT), Outcome 1: CTS symptoms (BCTQ)

Study or Subgroup	Splint Mean	Splint SD	Splint Total	ESWT Mean	ESWT SD	ESWT Total	Weight	Mean Difference IV, Random, 95% CI
10.1.1 Short-term improvement: 3 months or less								
Ulucakoy 2020	1.7	0.7	42	1.8	0.7	41	100.0%	-0.10 [-0.40 , 0.20]
Subtotal (95% CI)			**42**			**41**	**100.0%**	**-0.10 [-0.40 , 0.20]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.65 (P = 0.52)								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 10.2. Comparison 10: SPLINT VERSUS EXTRACORPOREAL SHOCK WAVE THERAPY (ESWT), Outcome 2: Function (BCTQ)

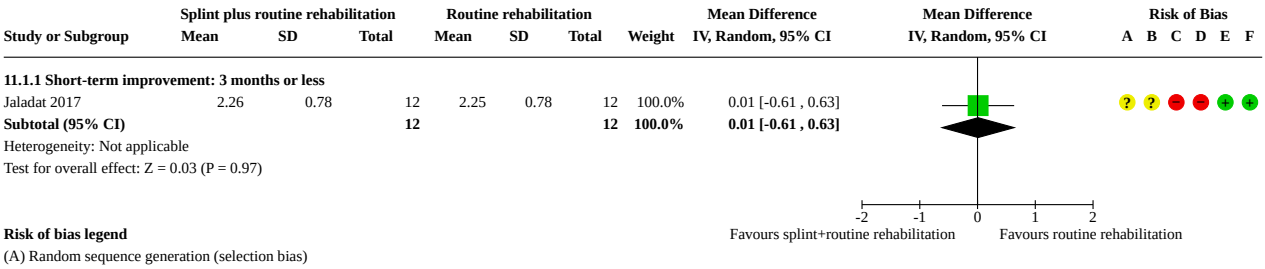


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Comparison 11. DYNAMIC SPLINT PLUS REHABILITATION VERSUS REHABILITATION

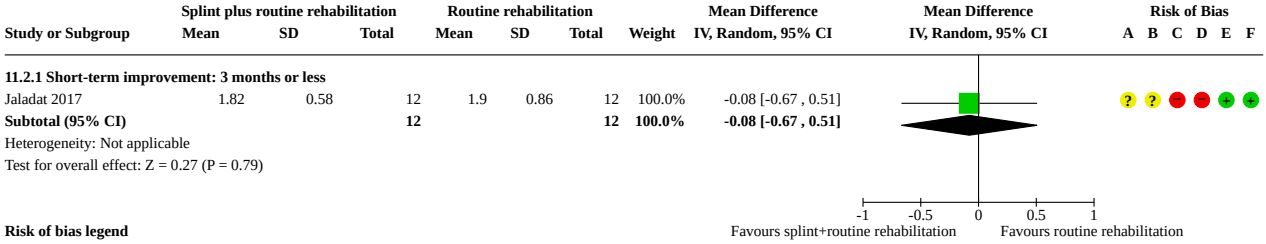
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
11.1 CTS symptoms (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
11.1.1 Short-term improvement: 3 months or less	1	24	Mean Difference (IV, Random, 95% CI)	0.01 [-0.61, 0.63]
11.2 Function (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
11.2.1 Short-term improvement: 3 months or less	1	24	Mean Difference (IV, Random, 95% CI)	-0.08 [-0.67, 0.51]

Analysis 11.1. Comparison 11: DYNAMIC SPLINT PLUS REHABILITATION VERSUS REHABILITATION, Outcome 1: CTS symptoms (BCTQ)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 11.2. Comparison 11: DYNAMIC SPLINT PLUS REHABILITATION VERSUS REHABILITATION, Outcome 2: Function (BCTQ)



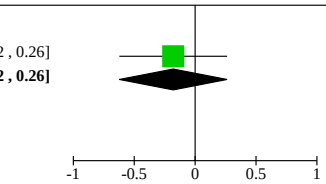
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Comparison 12. SPLINT SIX WEEKS VERSUS SPLINT 12 WEEKS

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12.1 CTS symptoms (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
12.1.1 Short-term improvement: 3 months or less	1	37	Mean Difference (IV, Random, 95% CI)	-0.18 [-0.62, 0.26]
12.2 Function (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
12.2.1 Short-term improvement: 3 months or less	1	37	Mean Difference (IV, Random, 95% CI)	0.05 [-0.39, 0.49]
12.3 Referral for surgery	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
12.3.1 Long-term improvement: over 3 months	1	37	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.12, 2.83]

Analysis 12.1. Comparison 12: SPLINT SIX WEEKS VERSUS SPLINT 12 WEEKS, Outcome 1: CTS symptoms (BCTQ)

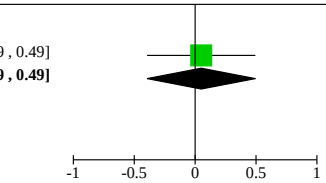
Study or Subgroup	Short term splinting Mean	SD	Total	Long term splinting Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F
12.1.1 Short-term improvement: 3 months or less										
Gatheridge 2020	1.99	0.59	17	2.17	0.78	20	100.0%	-0.18 [-0.62 , 0.26]		? + − − ? ?
Subtotal (95% CI)			**17**			**20**	**100.0%**	**-0.18 [-0.62 , 0.26]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.80 (P = 0.42)										



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 12.2. Comparison 12: SPLINT SIX WEEKS VERSUS SPLINT 12 WEEKS, Outcome 2: Function (BCTQ)

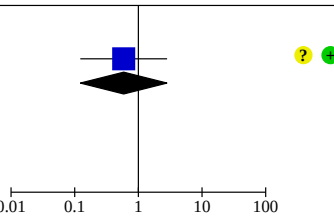
Study or Subgroup	Short term splinting Mean	SD	Total	Long term splinting Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F
12.2.1 Short-term improvement: 3 months or less										
Gatheridge 2020	1.65	0.64	17	1.6	0.74	20	100.0%	0.05 [-0.39 , 0.49]		? + − − ? ?
Subtotal (95% CI)			**17**			**20**	**100.0%**	**0.05 [-0.39 , 0.49]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.22 (P = 0.83)										



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 12.3. Comparison 12: SPLINT SIX WEEKS VERSUS SPLINT 12 WEEKS, Outcome 3: Referral for surgery

Study or Subgroup	Short term splinting Events	Total	Long term splinting Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F
12.3.1 Long-term improvement: over 3 months								
Gatheridge 2020	2	17	4	20	100.0%	0.59 [0.12 , 2.83]		? + − − ? ?
Subtotal (95% CI)		**17**		**20**	**100.0%**	**0.59 [0.12 , 2.83]**		
Total events:	2		4					
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.66 (P = 0.51)								



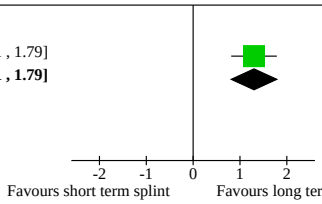
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Comparison 13. SPLINT SIX WEEKS VERSUS SPLINT SIX MONTHS

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13.1 CTS symptoms (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
13.1.1 Long-term improvement: > 3 months	1	156	Mean Difference (IV, Random, 95% CI)	1.30 [0.81, 1.79]
13.2 Function (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
13.2.1 Long-term improvement: > 3 months	1	156	Mean Difference (IV, Random, 95% CI)	2.30 [1.44, 3.16]
13.3 Referral for surgery	1	118	Risk Ratio (M-H, Random, 95% CI)	9.00 [0.50, 163.53]

Analysis 13.1. Comparison 13: SPLINT SIX WEEKS VERSUS SPLINT SIX MONTHS, Outcome 1: CTS symptoms (BCTQ)

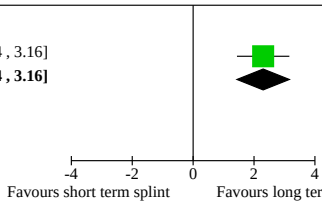
Study or Subgroup	Short term splinting Mean	SD	Total	Long term splinting Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
13.1.1 Long-term improvement: > 3 months								
Sanaee 2017	3.3	1.55	80	2	1.55	76	100.0%	1.30 [0.81 , 1.79]
Subtotal (95% CI)			**80**			**76**	**100.0%**	**1.30 [0.81 , 1.79]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.24 (P < 0.00001)								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 13.2. Comparison 13: SPLINT SIX WEEKS VERSUS SPLINT SIX MONTHS, Outcome 2: Function (BCTQ)

Study or Subgroup	Short term splinting Mean	SD	Total	Long term splinting Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
13.2.1 Long-term improvement: > 3 months								
Sanaee 2017	4.1	2.74	80	1.8	2.74	76	100.0%	2.30 [1.44 , 3.16]
Subtotal (95% CI)			**80**			**76**	**100.0%**	**2.30 [1.44 , 3.16]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.24 (P < 0.00001)								

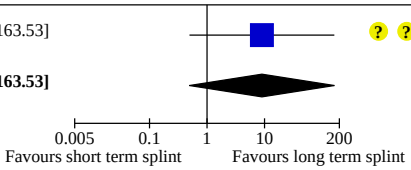


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 13.3. Comparison 13: SPLINT SIX WEEKS VERSUS SPLINT SIX MONTHS, Outcome 3: Referral for surgery

Study or Subgroup	Short term splint Events	Total	Long term splint Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F
Sanaee 2017	4	59	0	59	100.0%	9.00 [0.50 , 163.53]	? ? − − ? ?
Total (95% CI)		**59**		**59**	**100.0%**	**9.00 [0.50 , 163.53]**	
Total events:	4		0				

Heterogeneity: Not applicable
Test for overall effect: Z = 1.49 (P = 0.14)
Test for subgroup differences: Not applicable



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

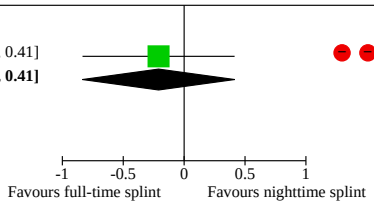
Comparison 14. NIGHT-TIME SPLINTING VERSUS FULL-TIME SPLINTING

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.1 CTS symptoms (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
14.1.1 Short-term improvement: 3 months or less	1	24	Mean Difference (IV, Random, 95% CI)	-0.21 [-0.83, 0.41]
14.2 Function (BCTQ)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
14.2.1 At the end of 6 weeks treatment	1	24	Mean Difference (IV, Random, 95% CI)	-0.21 [-0.87, 0.45]

Analysis 14.1. Comparison 14: NIGHT-TIME SPLINTING VERSUS FULL-TIME SPLINTING, Outcome 1: CTS symptoms (BCTQ)

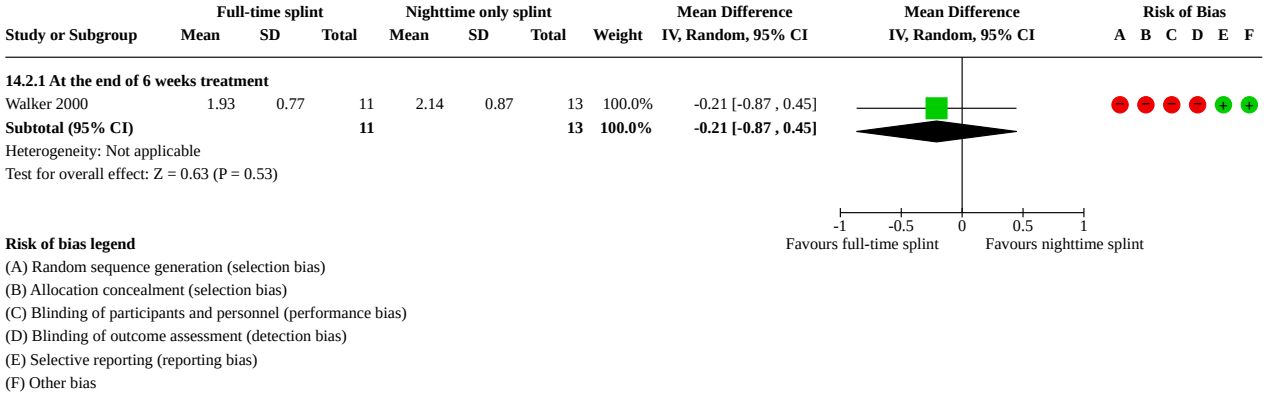
Study or Subgroup	Full-time splint Mean	SD	Total	Nighttime only splint Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F
14.1.1 Short-term improvement: 3 months or less									
Walker 2000	2.09	0.62	11	2.3	0.93	13	100.0%	-0.21 [-0.83 , 0.41]	− − − − + +
Subtotal (95% CI)			**11**			**13**	**100.0%**	**-0.21 [-0.83 , 0.41]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 14.2. Comparison 14: NIGHT-TIME SPLINTING VERSUS FULL-TIME SPLINTING, Outcome 2: Function (BCTQ)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Selective reporting (reporting bias)
(F) Other bias

ADDITIONAL TABLES

Table 1. SPLINT compared to NO ACTIVE TREATMENT for carpal tunnel syndrome - outcomes that are not presented in the summary of findings table

SPLINT compared to NO ACTIVE TREATMENT for carpal tunnel syndrome - outcomes that are not presented in the summary of findings table

Patient or population: carpal tunnel syndrome
Setting: outpatient clinics in Italy, Thailand and Turkey; hospital clinic in Australia; education and research hospital in Turkey
Intervention: SPLINT
Comparison: NO ACTIVE TREATMENT

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with NO ACTIVE TREATMENT	Risk with SPLINT				
Functional status (Boston CTS questionnaire) - short-term improvement: < 3 months. Scale: 1 to 5, higher is worse	The mean function was **1.97** points	MD **0.24 points better** (0.44 better to 0.03 better)	-	306 (6 RCTs)	⊕⊕⊕⊖ **Moderate**[a]	Splint probably does not improve hand function in the short term. Absolute difference 6% better (11% better to 0.75% better) with splint
Overall improvement - long-term improvement: > 3 months	No studies reported this outcome		-	(0 RCTs)	-	Not estimable. We are uncertain about the effect.
Health-related quality of life - short-term improvement: < 3 months	No studies reported this outcome		-	(0 RCTs)	-	Not estimable. We are uncertain about the effect.

*__The risk in the intervention group__ (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD**: mean difference; **RCT**: randomised controlled trial; **RR:** risk ratio; **CTS**: carpal tunnel syndrome

GRADE Working Group grades of evidence

Table 1. SPLINT compared to NO ACTIVE TREATMENT for carpal tunnel syndrome - outcomes that are not presented in the summary of findings table *(Continued)*

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]Downgraded for high risk of bias in the included studies (lack of blinding)

APPENDICES

Appendix 1. Cochrane Neuromuscular Specialised Register via CRS-Web search strategy

1 MeSH DESCRIPTOR Carpal Tunnel Syndrome AND INREGISTER 373

2 "carpal tunnel" AND INREGISTER 595

3 ("nerve entrapment" or "nerve compression" or "entrapment neuropathy" or "entrapment neuropathies") and carpal AND INREGISTER 43

4 #1 or #2 or #3 595

5 MeSH DESCRIPTOR Splints AND INREGISTER 74

6 MeSH DESCRIPTOR Braces AND INREGISTER 13

7 splint* or brace* or "wrist support*" AND INREGISTER 185

8 #5 or #6 or #7 185

9 #4 and #8 146

Appendix 2. Cochrane Central Register of Controlled Trials (CENTRAL) via CRS-Web search strategy

1 MeSH DESCRIPTOR Carpal Tunnel Syndrome AND CENTRAL:TARGET 756

2 "carpal tunnel" AND CENTRAL:TARGET 1694

3 ("nerve entrapment" or "nerve compression" or "entrapment neuropathy" or "entrapment neuropathies") and carpal AND CENTRAL:TARGET 127

4 #1 or #2 or #3 1694

5 MeSH DESCRIPTOR Splints AND CENTRAL:TARGET 465

6 MeSH DESCRIPTOR Braces AND CENTRAL:TARGET 437

7 splint* or brace* or "wrist support*" AND CENTRAL:TARGET 4811

8 #5 or #6 or #7 4811

9 #4 and #8 321

10 INREGISTER 7877

11 #9 NOT #10 179

Appendix 3. MEDLINE (OvidSP) search strategy

Database: Ovid MEDLINE(R) ALL <1946 to December 10, 2021>

1 (randomized controlled trial or controlled clinical trial).pt. or (randomi?ed or placebo or randomly or trial or groups).ab. or drug therapy.fs. (5214596)

2 exp animals/ not humans.sh. (4923984)

3 1 not 2 (4539025)

4 Carpal Tunnel Syndrome.tw. or Carpal Tunnel Syndrome/ or ((nerve entrapment or nerve compression or entrapment neuropath*) and carpal).mp. (11693)

5 SPLINTS/ or BRACES/ or (SPLINT* or BRACE* or WRIST SUPPORT*).tw. (30013)

6 3 and 4 and 5 (208)

7 limit 6 to ed=20201211-20211231 (6)

8 limit 6 to dt=20201211-20211231 (7)

9 7 or 8 (13)

Appendix 4. Embase (OvidSP) search strategy

Database: Embase <1974 to 2021 Week 49>

1 Randomized controlled trial/ or Controlled clinical study/ or randomization/ or intermethod comparison/ or double blind procedure/ or human experiment/ or (random$ or placebo or (open adj label) or ((double or single or doubly or singly) adj (blind or blinded or blindly)) or parallel group$1 or crossover or cross over or ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention $1 or patient$1 or subject$1 or participant$1)) or assigned or allocated or (controlled adj7 (study or design or trial)) or volunteer or volunteers).ti,ab. or (compare or compared or comparison or trial).ti. or ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. (5590987)

2 limit 1 to (conference abstracts or embase) (4778818)

3 carpal tunnel syndrome/ or carpal tunnel syndrome.tw. or ((nerve entrapment or nerve compression or entrapment neuropath*) and carpal).mp. (17327)

4 splint/ or brace/ or (splint* or brace* or wrist support*).tw. (34265)

5 2 and 3 and 4 (252)

6 limit 5 to em=202050-202149 (18)

Appendix 5. AMED (OvidSP) search strategy

Database: AMED (Allied and Complementary Medicine) <1985 to December 2021>

1 Randomized controlled trials/ or Random allocation/ or Double blind method/ or Single-Blind Method/ or exp Clinical Trials/ or (clin* adj25 trial*).tw. or ((singl* or doubl* or treb* or trip*) adj25 (blind* or mask* or dummy)).tw. or placebos/ or placebo*.tw. or random*.tw. or research design/ or Prospective Studies/ or meta analysis/ or (meta?analys* or systematic review*).tw. or control*.tw. or (multicenter or multicentre).tw. or ((study or studies or design*) adj25 (factorial or prospective or intervention or crossover or cross-over or quasi-experiment*)).tw. (67795)

2 carpal tunnel syndrome/ or carpal tunnel syndrome.tw. or ((nerve entrapment or nerve compression or entrapment neuropath*) and carpal).mp. (592)

3 splints/ or braces/ or (splint* or brace* or wrist support*).tw. (1526)

4 1 and 2 and 3 (40)

5 limit 4 to yr="2020 -Current" (6)

Appendix 6. CINAHL (EBSCOhost) search strategy

Sunday, December 12, 2021 9:02:00 PM

S8 S6 AND S7 1

S7 EM 20180601- Limiters - Exclude MEDLINE records 241,618

S6 S3 and S4 and S5 121

S5 (MH "Splints") OR splint* or brace* or "wrist support*" 12,412

S4 (MH "Carpal Tunnel Syndrome") OR "carpal tunnel syndrome" OR ("nerve entrapment" and carpal) OR ("nerve compression" and carpal) OR ("entrapment neuropath*" and carpal) 3,854

S3 S1 NOT S2 876,076

S2 (MH Animals+ OR MH (Animal Studies) OR TI (Animal Model*)) NOT MH (Human) 199,936

S1 MH ("Randomized Controlled Trials" OR "Double-Blind Studies" OR "Single-Blind Studies" OR "Random Assignment" OR "Pretest-Posttest Design" OR "Cluster Sample" OR "Placebos" OR "Crossover Design" OR "Comparative Studies") OR TI (Randomised OR Randomized OR Trial) OR AB (Random* OR (Control W5 Group) OR (Cluster W3 RCT)) OR (MH ("Sample Size") AND AB (Assigned OR Allocated OR Control)) OR PT (Randomized Controlled Trial) 919,968

Appendix 7. ClinicalTrials.Gov search strategy

Advanced Search

Condition or disease: Carpal Tunnel Syndrome

Study type: Interventional Studies (Clinical Trials)

Intervention/treatment: Splint* OR Brace* OR Wrist Support*

3 Studies found

Appendix 8. WHO ICTRP search strategy

Advanced Search

Carpal Tunnel Syndrome *in the Condition*

Splint* OR Brace* OR Wrist Support* *in the Intervention*

Recruitment status is ALL

77 records for 77 trials found

WHAT'S NEW

Date	Event	Description
27 February 2023	New search has been performed	Based on an updated search, 20 new studies were included in the review (Akturk 2018; Boonhong 2017; Chesterton 2018; De Moraes 2021; Eraslan 2014; Gatheridge 2020; Geler Kulcu 2016; Hall 2013; Jaladat 2017; Kocaoglu 2017; Oncu 2014; Rioja Toro 2012; Sanaee 2017; Schmid 2012; So 2018; Ulucakoy 2020; Wang 2017; Willis 2016; Wu 2017; Yazdanpanah 2012); eight studies, included in the previous version of this review, remain included (De Entrambasaguas 2006; Madjdinasab 2008; Manente 2001; Mishra 2006; Premoselli 2006; Sevim 2004; Walker 2000; Werner 2005); one study, which was awaiting classification in the previous version of this review, is now included (Taspinar 2007).
27 February 2023	New citation required and conclusions have changed	Data, which were not pooled in meta-analysis in the previous version of this review, are now combined (i.e. Manente 2001 and- Premoselli 2006 at short-term analysis). The previous version of this review did not include any data from Sevim 2004 in analysis, but we have included them. We excluded the following comparisons (included in the previous version of this review):

Date	Event	Description
		• Different splint designs were excluded until splints show efficacy since all identified comparisons tested some specific splint against another specific splint and inference to other splints is limited; • Splint versus interventions that are unlikely disease modifying or it was impossible isolate the effect of splint (splint versus yoga; splint verus acupuncture; splint plus nerve and tendon gliding exercises with gabapentin plus nerve and tendon gliding exercises; splint plus steroid injection versus therapeutic ultrasound; splint plus steroid injection plus nerve and tendon gliding exercises versus nerve and tendon gliding exercises; splint plus steroid injection versus nerve and tendon gliding exercises; splint plus NSAID versus local corticosteroid injection). Changes to outcomes: • The primary outcome is amended from "short-term overall improvement" (in the previous version of this review) to "CTS symptoms" because the included studies did not measure this outcome in the previous review and preliminary overview (before data extraction) suggested that this outcome is rarely measured and reported. • We excluded "improvement in neurophysiologic parameters" from the outcomes since they are not patient-important outcomes. • We added "referral to surgery" as an outcome, because it may be important outcome in clinical decision making.

HISTORY

Review first published: Issue 7, 2012

CONTRIBUTIONS OF AUTHORS

TEEMU KARJALAINEN (TK) was involved in the design of the update; screening of the search results and assessing retrieved full texts, appraising risk of bias; extracting data; performing analyses; interpreting analyses including certainty of evidence; and writing of the review.

VIEDA LUSA (VL) was involved in the screening of the search results and assessing retrieved full texts, appraising the risk of bias; extracting data; performing analyses; interpreting the evidence, including certainty of evidence; and writing of the review.

SUSAN PETERS (SP) screening of the search results and assessing retrieved full texts, appraising risk of bias; extracting data; performing analyses; interpreting the evidence, including certainty of evidence; and writing of the review.

MATTHEW PAGE (MP) was involved in the following stages of the review: appraising the risk of bias of papers; extracting data from papers; editing the review.

NICOLA MASSY-WESTROPP (NMW) was involved in the following stages of the review: appraising the risk of bias of papers; extracting data from papers; approval of the final review.

DENISE O'CONNOR (DOC) was responsible for: appraising the risk of bias of papers; extracting data from papers; approval of the final review.

DECLARATIONS OF INTEREST

TVK declares no conflicts of interests in this review. As a consultant in hand surgery, he frequently sees and treats people with carpal tunnel syndrome in a public hospital (salaried position). He also receives remuneration for private practice.

VL declares no conflicts of interests in this review.

MJP declares no conflicts of interests in this review.

NMW declares no conflicts of interests in this review. She is an Interplast Australia Volunteer presenter of hand therapy and anatomy webinars and direct hand therapy training and a volunteer research advocacy and education committee member for Arthritis South Australia, volunteer research committee member for Australian Hand Therapy Association.

DOC declares no conflicts of interests in this review. She is an Editor, Cochrane EPOC, Director, Cochrane EPOC Australasian Satellite and Editor, Cochrane Musculoskeletal.

SEP declares no conflicts of interests in this review.

SOURCES OF SUPPORT

Internal sources

- No sources of support provided

External sources

- Teemu Karjalainen, Finland

  TK is supported by a Finnish Medical Foundation research grant.
- Vieda Lusa, Finland

  Vieda Lusa is supported by Hospital Nova Foundation (Sairaala Novan säätiö) research grant.
- Cochrane Neuromuscular, UK

  This project was supported by the National Institute for Health and Care Research (NIHR) via Cochrane Infrastructure funding to Cochrane Neuromuscular. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health. Cochrane Neuromuscular is also supported by the Queen Square Centre for Neuromuscular Diseases.
- Matthew Page, Australia

  Matthew J Page is supported by an Australian Research Council Discovery Early Career Award (DE200101618).
- Susan Peters, USA

  Susan Peters is supported by funding recieved from the National Institute for Occupational Safety and Health (U19 OH008861).
- Denise O'Connor, Australia

  Denise O'Connor is supported by an Australian National Health and Medical Research Council (NHMRC) Public Health Fellowship (#606726).

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In this update, we did not include neurophysiological parameters. We also changed symptoms (continuous outcome) as the primary outcome as only one paper had measured overall improvement (binary outcome). Changes to outcomes were as follows.

- The primary outcome was amended from "short-term overall improvement" (in the previous version of this review) to "CTS symptoms" because the included studies did not measure this outcome in the previous review and a preliminary overview (before data extraction) suggested that this outcome is rarely measured and reported.
- We excluded "improvement in neurophysiologic parameters" since they are not patient-important outcomes.
- We added "referral to surgery", because it may be important in clinical decision-making.

We excluded the following comparisons included in the previous version of this review.

- Different splint designs were excluded until splints show efficacy since all identified comparisons tested some specific splint against another specific splint and inference to other splints was limited;
- Splint versus interventions that are unlikely to be disease-modifying or it was impossible to isolate the effect of the splint (splint versus yoga; splint verus acupuncture; splint plus nerve and tendon gliding exercises with gabapentin plus nerve and tendon gliding exercises; splint plus steroid injection versus therapeutic ultrasound; splint plus steroid injection plus nerve and tendon gliding exercises versus nerve and tendon gliding exercises; splint plus steroid injection versus nerve and tendon gliding exercises; splint plus NSAIDs versus local corticosteroid injection).

For the first version of the splints review, the primary outcome (see Page 2012b) was short-term overall improvement (any measure in which patients indicate the intensity of their complaints compared with baseline) (three months or less; reported as a dichotomous outcome). Secondary outcomes were as follows.

1. Adverse effects.
2. Short-term improvement in CTS symptoms (for example, pain, paraesthesia, nocturnal paraesthesia) (three months or less).
3. Short-term improvement in functional ability or health-related quality of life (three months or less).
4. Short-term improvement in neurophysiologic parameters (three months or less).
5. Long-term improvement in CTS symptoms (greater than three months).
6. Long-term improvement in functional ability or health-related quality of life (greater than three months).

In the original version of the review, Non-surgical interventions for carpal tunnel syndrome by O'Connor and colleagues (O'Connor 2003), types of outcome measures were as follows.

The primary outcome measure was improvement in clinical symptoms, such as pain and paraesthesiae, at least three months after the end of treatment.

Secondary outcome measures included:

1. Improvement in functional status and/or health-related quality of life parameters at least three months after treatment;
2. Improvement in objective physical examination measures, such as grip, pinch strength, and sensory perception at least three months after treatment;
3. Improvement in neurophysiological parameters three months after treatment;
4. Clinical improvement at less than three months of follow-up;
5. Clinical improvement at one year after treatment;
6. Need for surgical release of the flexor retinaculum during follow-up.

INDEX TERMS

Medical Subject Headings (MeSH)

*Carpal Tunnel Syndrome [therapy]; Hand; *Occupational Therapy; Quality of Life; Upper Extremity

MeSH check words

Adult; Humans; Middle Aged