ClinicalEvidence

Carpal tunnel syndrome

Search date March 2009

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ABSTRACT

INTRODUCTION: Carpal tunnel syndrome is a neuropathy caused by compression of the median nerve within the carpal tunnel. However, the severity of symptoms and signs does not often correlate well with the extent of nerve damage. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of drug treatments, non-drug treatments, surgical treatments, and postoperative treatments for carpal tunnel syndrome? We searched: Medline, Embase, The Cochrane Library, and other important databases up to March 2009 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 53 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: acupuncture, carpal tunnel release surgery (open and endoscopic), diuretics, internal neurolysis, local and systemic corticosteroids, massage therapy, nerve and tendon gliding exercises, non-steroidal anti-inflammatory drugs (NSAIDs), pyridoxine, therapeutic ultrasound, and wrist splints.

QUESTIONS

INTERVENTIONS

Key points

- Carpal tunnel syndrome is a neuropathy caused by compression of the median nerve within the carpal tunnel.

  Classic symptoms include numbness, tingling, burning, or pain in at least two of the three digits supplied by the median nerve (i.e., the thumb and the index and middle fingers).

Symptoms can resolve within 6 months in about one third of people — particularly younger people — whereas poor prognosis is often indicated by bilateral symptoms and a positive Phalen's test. However, the severity of symptoms and signs does not often correlate well with the extent of nerve damage.

- Corticosteroid treatment (either local injection or systemic) seems beneficial in treating carpal tunnel syndrome, although the evidence suggests that there is greater improvement in outcomes with local injections compared with systemic administration.

  Risks associated with local corticosteroid injections into the carpal tunnel include tendon rupture and injection into the median nerve.

  Systemic corticosteroids commonly cause nausea, anxiety, acne, menstrual irregularities, insomnia, headaches, and mood swings. They can also cause peptic ulcer, corticosteroid psychosis, osteoporosis, and adrenal insufficiency.
- We don't know whether diuretics, non-steroidal anti-inflammatory drugs (NSAIDs), or pyridoxine are effective in treating carpal tunnel syndrome, because the RCTs identified have been too small to draw reliable conclusions.
- We don't know whether therapeutic ultrasound or wrist splints are effective in relieving symptoms of carpal tunnel syndrome. We also don't know whether acupuncture or massage therapy are effective at relieving symptoms of carpal tunnel syndrome, as there have been no RCTs of these interventions.
- Nerve and tendon gliding exercises may be no more effective than wrist splints at relieving symptoms and improving hand function in people with carpal tunnel syndrome.
- We found insufficient RCT evidence to assess whether surgery is more effective than no treatment.

  Surgery seems to improve clinical outcomes compared with wrist splints.

  We don't know whether surgery is as effective as local corticosteroid injections.

  Both endoscopic and open carpal tunnel release seem to improve symptoms, although the data are unclear as to which is more beneficial. Both are associated with several adverse effects.

  Internal neurolysis in conjunction with open carpal tunnel release does not seem to relieve symptoms compared with open carpal tunnel release alone.
- Wrist splinting after carpal tunnel release surgery has no effect on symptoms of carpal tunnel syndrome or hand function.

DEFINITION

Carpal tunnel syndrome (CTS) is a neuropathy caused by compression of the median nerve within the carpal tunnel. [1] Classical symptoms of CTS include numbness, tingling, burning, or pain in at least two of the three digits supplied by the median nerve (i.e., the thumb and the index and middle fingers). [2] The American Academy of Neurology has described diagnostic criteria that rely on a combination of symptoms and physical examination findings. [3] Other diagnostic criteria include results from electrophysiological studies. [2]

INCIDENCE/ PREVALENCE

A general population survey in Rochester, Minnesota, found the age-adjusted incidence of CTS to be 105 (95% CI 99 to 112) cases per 100,000 person years. [4] [5] Age-adjusted incidence rates were 52 (95% CI 45 to 59) cases per 100,000 person years for men and 149 (95% CI 138 to 159) cases per 100,000 person years for women. The study found that incidence rates increased from 88 (95% CI 75 to 101) cases per 100,000 person years between 1961 and 1965 to 125 (95% CI 112 to 138) cases per 100,000 person years between 1976 and 1980. Incidence rates of CTS increased with age for men, whereas for women they peaked between the ages of 45 and 54 years. A general population survey in the Netherlands found prevalence to be 1% for men and 7% for women. [6] A more comprehensive study in southern Sweden found that the general population prevalence for CTS was 3% (95% CI 2% to 3%). [7] As in other studies, the overall prevalence in women was higher than in men (male to female ratio 1.0:1.4); however, among older people, the prevalence in women was almost four times that in men (age group 65–74 years: men 1%, 95% CI 0% to 4%; women 5%, 95% CI 3% to 8%). Over 50% of pregnant women develop symptoms of CTS. [8] [9] However, many trials exclude pregnant women, and we have not identified any RCTs assessing the treatment of pregnancy-induced CTS. The pathophysiology of idiopathic and pregnancy-induced CTS are likely to differ, with one key consideration in pregnancy-induced CTS being fluid retention. Therefore, strategies to reduce fluid retention will probably be of more benefit in pregnancy-induced CTS than they have been shown to be in idiopathic CTS.

AETIOLOGY/ RISK FACTORS

Most cases of CTS have no easily identifiable cause (idiopathic). [4] Secondary causes of CTS include the following: space-occupying lesions (tumours, hypertrophic synovial tissue, fracture callus, and osteophytes), metabolic and physiological (pregnancy, hypothyroidism, and rheumatoid arthritis), infections, neuropathies (associated with diabetes mellitus or alcoholism), and familial disorders. [4] One case control study found that risk factors in the general population included repetitive activities requiring wrist extension or flexion, obesity, rapid dieting, shorter height, hysterectomy without oophorectomy, and recent menopause. [10]

PROGNOSIS One observational study (CTS defined by symptoms and electrophysiological study results) found that 34% of people with idiopathic CTS without treatment had complete resolution of symptoms (remission) within 6 months of diagnosis. [11] Remission rates were higher for younger age groups and for women. One observational study in pregnant women found that, in most cases, pregnancy-induced CTS spontaneously improved after delivery. However, some women complained of symptoms of CTS 1 year after delivery. [9] A more recent observational study of untreated idiopathic CTS also showed that symptoms can spontaneously resolve in some people. The main positive prognostic indicators were short duration of symptoms and young age, whereas bilateral symptoms and a positive Phalen's test were indicators of a poorer prognosis. [12]

AIMS OF INTERVENTION To improve symptoms and reduce the physical signs of CTS; to prevent progression and loss of hand function secondary to CTS; to minimise loss of time from work.

OUTCOMES Symptom severity; hand function; time to return to work.

METHODS *Clinical Evidence* search and appraisal March 2009. The following databases were used to identify studies for this systematic review: Medline 1966 to March 2009, Embase 1980 to March 2009, and The Cochrane Library, issue 1, 2009 (for the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects [DARE], and the Health Technology Assessment [HTA] database 1966 to date). We also searched for retractions of studies included in the review. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the contributor for additional assessment, using pre-determined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews of RCTs and RCTs in any language. RCTs of drugs, ultrasound, and acupuncture had to be at least single-blinded where possible; we excluded all studies described as "open", "open label", or not blinded, unless blinding was impossible. For all other treatments, RCTs without a blinded control group were considered. RCTs had to contain 20 or more individuals. The minimum length of follow-up required to include studies was 1 month. There was no maximum loss to follow-up required to include studies. We excluded studies of acupuncture that did not use needles. We included systematic reviews of RCTs and RCTs where harms of an included intervention were studied, applying the same study design criteria for inclusion as we did for benefits. In addition we use a regular surveillance protocol to capture harms alerts from organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which are added to the reviews as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 27).

QUESTION What are the effects of drug treatments for carpal tunnel syndrome?

OPTION CORTICOSTEROIDS (LOCAL INJECTION)

Symptom severity

Compared with placebo or no treatment Local corticosteroid injection seems more effective at improving symptoms of carpal tunnel syndrome after 2 to 6 weeks (moderate-quality evidence).

Compared with systemic steroids Local corticosteroid injection may be more effective at improving symptom severity after 4 to 12 weeks (low-quality evidence).

Compared with carpal tunnel release surgery We don't know whether local corticosteroid injection is more effective at improving symptoms of CTS (low-quality evidence).

Hand function

Compared with carpal tunnel release surgery Local corticosteroid injection may be equally effective at improving hand function in people with CTS (moderate-quality evidence).

Adverse effects

Known risks associated with local corticosteroid injection into the carpal tunnel include tendon rupture and injection into the median nerve.

For GRADE evaluation of interventions for carpal tunnel syndrome, see table, p 27 .

Benefits: We found two systematic reviews (search dates 2006). [13] [14]

Local corticosteroid injection versus placebo or no treatment:
The two systematic reviews [13] [14] each identified three RCTs comparing local corticosteroid injection versus placebo injection or no treatment; two RCTs were common to both reviews. The first systematic review pooled data for the common two RCTs, but did not specify why results from the third RCT were not pooled. [13] The second systematic review did not pool data because of clinical heterogeneity among RCTs. [14]

The first systematic review found that local corticosteroid injection significantly increased the proportion of people with clinical improvement at 1 month or less compared with placebo (2 RCTs; 141 people with CTS: 53/73 [73%] with local corticosteroid injection *v* 19/68 [28%] with placebo injection; RR 2.58, 95% CI 1.72 to 3.87). [13] One RCT measured clinical improvement by subjective report of clinical severity at 1 month, and the other RCT measured patient satisfaction with the degree of symptom relief using a 5-point scale at 2 weeks. [13] The 2-week follow-up period for the second RCT is very short; it represents a significant limitation to the study, and does not meet the *Clinical Evidence* review criteria of follow-up of at least 1 month.

The other RCT [15] identified by the first systematic review [13] (84 people) compared low-dose local corticosteroid injection (hydrocortisone 25 mg) versus high-dose local corticosteroid injection (hydrocortisone 100 mg) versus no treatment. It found that both low- and high-dose hydrocortisone significantly increased the proportion of people with improved symptoms at 6 weeks, compared with no treatment (21/32 [66%] with low-dose hydrocortisone *v* 1/20 [5%] with no injection; RR 13.1, 95% CI 1.9 to 90.1; NNT 2, 95% CI 2 to 3; 20/32 [63%] with high-dose hydrocortisone *v* 1/20 [5%] with no injection; RR 12.5, 95% CI 1.8 to 86.0; NNT 2, 95% CI 2 to 4). [15] The RCT found no significant difference between high and low doses of hydrocortisone in the proportion of people with improvement at 6 weeks (proportion of people describing symptoms as "better" or "much better" at 6 weeks: 21/32 [66%] with low-dose hydrocortisone *v* 20/32 [63%] with high-dose hydrocortisone; P greater than 0.5; RR 1.0, 95% CI 0.7 to 1.5). However, caution should be used in interpreting these results because the RCT did not quantify the terms "better" or "much better", and changes in individual symptoms were not described.

The other RCT [16] identified by the second systematic review [14] (32 people; 53 nerves) compared methylprednisolone 15 mg injected locally versus the same amount of saline injected locally. Injections were repeated after 1 week. The RCT did not perform direct between-group comparisons, but compared results at 2 months versus baseline results; hence the results should be treated with caution. The RCT found that in the corticosteroid group, paraesthesias, pain, and motor deficit were significantly improved at 2 months compared with baseline (P less than 0.0001 for paraesthesias; P less than 0.0001 for pain; P less than 0.005 for motor deficit). However, in the placebo group, there were no significant differences between baseline and 2 months (reported as not significant; P values not reported). The RCT found that in both the corticosteroid and placebo groups, nocturnal acroparaesthesias at 2 months were significantly improved compared with baseline (P less than 0.0001 with corticosteroid; P less than 0.005 with placebo). The RCT found no significant differences between baseline and 2 months in hypaesthesia and weakness for both the corticosteroid and placebo groups (reported as not significant; P values not reported). No absolute values were reported for any of the outcomes listed. The RCT measured signs (weakness, atrophy, and hypaesthesia) and symptoms (paraesthesias, nocturnal acroparaesthesias, pain, and motor deficit) of CTS using a subjective scoring system of 0 to 4 (where 0 = absent signs or symptoms and 4 = marked signs or symptoms).

Local corticosteroid injection versus systemic corticosteroids:
The first systematic review [13] identified two RCTs, [17] [18] and the second systematic review [14] identified one common RCT, [18] comparing local corticosteroid injection versus systemic corticosteroids. The first systematic review did not pool data; the RCTs assessed different outcomes at different time frames.

The first RCT [17] identified by the first systematic review [13] (37 women) compared local corticosteroid injection (betamethasone 1.5 mg) into the carpal tunnel of the more severely affected hand plus placebo (saline) injection into the deltoid muscle of the same side versus local placebo injection into the carpal tunnel plus corticosteroid injection (betamethasone 1.5 mg) into the deltoid muscle. It found that local corticosteroid injection significantly improved symptom severity after 1 month compared with systemic corticosteroid injection (clinical improvement: 9/18 [50%] with local injection *v* 3/19 [16%] with systemic injection; RR 3.17, 95% CI 1.02 to 9.87). [17] It should be noted that the RCT only defined clinical outcomes loosely, using a subjective ordinal ranking scale, and failed to specify the magnitude of symptomatic improvement or the changes in specific symptoms.

The second RCT [18] common to both reviews (60 people) [13] [14] compared a single local corticosteroid injection (methylprednisolone 15 mg) plus oral placebo versus oral corticosteroid (prednisolone 25 mg/day for 10 days) plus placebo injection. It found no significant difference between

local corticosteroid injection and systemic corticosteroids in mean Global Symptom Scores (GSS) after 2 weeks, but found a significant improvement with local corticosteroid injection after 8 and 12 weeks (GSS, WMD, 2 weeks: –4.2, 95% CI –8.7 to +0.3; 8 weeks: –7.2, 95% CI –11.5 to –2.9; 12 weeks: –7.0, 95% CI –11.6 to –2.4). [18]

Local corticosteroid injection versus surgery:
See benefits of surgery, p 16

Harms:

Local corticosteroid injection versus placebo or no treatment:
The first systematic review did not specifically assess adverse events, but reported no adverse effects in the two RCTs common to both reviews. [13] The second systematic review, the other RCT [15] identified by the first systematic review, [13] and the other RCT [16] identified by the second systematic review [14] did not report on harms of treatment. Known risks associated with local corticosteroid injection into the carpal tunnel include tendon rupture and injection into the median nerve. [19]

Local corticosteroid injection versus systemic corticosteroids:
The first RCT [17] identified by the first systematic review [13] did not report on harms of treatment. The second RCT [18] common to both reviews [13] [14] reported nine adverse effects with oral prednisolone plus placebo injection: bloating (2 people), insomnia (2 people), polyphagia (3 people), and injection pain (2 people). [18] The RCT also reported that two people had injection pain in the local corticosteroid injection group. [18]

Local corticosteroid injection versus surgery:
See harms of surgery, p 16

Comment:

We identified one RCT comparing corticosteroid injection versus night-time splint versus physiotherapy (ultrasound or TENS), which will be considered for inclusion once translated. [20]

Clinical guide:
We don't know which corticosteroid, at what dose and volume, and which injection technique is most effective. More studies are needed to support the role of corticosteroid injection in the continuum of care in CTS. Many clinicians would probably agree that local corticosteroid injection is useful in pregnancy, in flares of disease activity, or if surgery is delayed for some reason. However, long-term corticosteroid use can be associated with some, as yet unquantified, risks. One common concern is that, although corticosteroids improve symptoms, underlying damage to the median nerve could occur.

OPTION CORTICOSTEROIDS (SYSTEMIC)

Symptom severity
Compared with placebo Systemic corticosteroids seem more effective at improving symptoms of CTS at 4 and 8 weeks (moderate-quality evidence).

Compared with local corticosteroid injections Systemic corticosteroids may be less effective at improving symptoms after 4 to 12 weeks than local corticosteroid injections (low-quality evidence).

Compared with NSAIDs Systemic corticosteroids seem more effective at improving symptoms of CTS at 4 weeks (moderate-quality evidence).

Compared with diuretics Systemic corticosteroids may be more effective at reducing symptoms of CTS (very low-quality evidence).

Compared with splints We don't know whether systemic corticosteroids are more effective at improving symptoms of CTS at 3 months (low-quality evidence).

Hand function
Compared with splints Systemic corticosteroids may be more effective at improving hand function in people with CTS after 3 months (low-quality evidence).

Adverse effects
Systemic corticosteroids commonly cause nausea, anxiety, acne, menstrual irregularities, insomnia, headaches, and mood swings. They can also cause peptic ulcer, corticosteroid psychosis, osteoporosis, and adrenal insufficiency.

For GRADE evaluation of interventions for carpal tunnel syndrome, see table, p 27 .

Benefits:

Systemic corticosteroids versus placebo:
We found one systematic review (search date 2002) comparing systemic corticosteroids versus placebo. [21] The review found that oral corticosteroids (prednisolone or prednisone for 10 days–4 weeks) significantly improved symptoms compared with placebo at 4 and 8 weeks (Global Symptom Score (GSS) at 4 weeks: 1 RCT, 39 people; 23 with systemic corticosteroids *v* 16 with placebo; WMD –10.80, 95% CI –15.26 to –6.34; GSS at 8 weeks: 2 RCTs, 51 people; combined GSS for both RCTs not reported; mean difference –6.46, 95% CI –11.93 to –0.99). [21]

Systemic corticosteroids versus local corticosteroid injection:
See benefits of corticosteroids (local injection), p 3 .

Systemic corticosteroids versus NSAIDs:
We found one systematic review (search date 2002), [21] which identified one RCT (91 people) [22] comparing oral prednisolone (20 mg/day for 2 weeks followed by 10 mg/day for another 2 weeks; 26 people), an oral slow-release NSAID (tenoxicam 20 mg/day; 22 people), an oral diuretic (trichlormethiazide 2 mg/day; 20 people), and placebo (23 people). It found that prednisolone significantly improved GSS compared with tenoxicam at 4 weeks (24 with systemic corticosteroids *v* 10 with NSAIDs; mean difference 14.00, 95% CI 8.57 to 19.43). [21]

Systemic corticosteroids versus diuretics:
See benefits of diuretics, p 7 .

Systemic corticosteroids versus splints:
We found one RCT (40 people, 71 hands) comparing oral prednisolone (20 mg/day for 2 weeks, followed by 10 mg/day for a further 2 weeks) with commercially available neutral wrist splints (advised to be worn during the night and as much as possible during the day). [23] Symptom severity and functional status were assessed using a 5-point scoring system (1 = no symptom or no difficulty to 5 = severe symptoms preventing the activity). Symptom severity incorporated 11 items (relating to pain, nocturnal symptoms, numbness, tingling, and weakness) and functional status eight items associated with daily tasks (e.g., difficulty in writing, opening jars, and holding a book). The RCT found that oral corticosteroids significantly improved functional score compared with wrist splints after 1 month (mean change from baseline functional score after 1 month: 0.23 with oral corticosteroid *v* 0.14 with wrist splint; P = 0.01). Significance was maintained at 3 months (mean change in baseline functional score after 3 months: 0.26 with oral corticosteroid *v* 0.16 with wrist splint; P = 0.03). However, these results should be interpreted with caution, because the study did not carry out a correction for multiple statistical testing. The RCT found no significant difference in Symptom Severity Scale score between oral corticosteroids and wrist splint after 3 months (mean change from baseline symptom severity score: 0.49 with oral corticosteroid *v* 0.39 with wrist splint; P = 0.42).

Harms:

Systemic corticosteroids versus placebo:
One RCT [22] identified by the review [21] found that adverse effects included nausea and epigastric pain (nausea: 3/23 [13%] people with prednisolone *v* 1/16 [6%] people with placebo; epigastric pain: 2/23 [9%] of people with prednisolone *v* 2/16 [13%] of people with placebo). However, these results should be interpreted with caution because 18/91 (20%) people did not complete the trial, and analysis of data was not by intention to treat. [22] The other RCT [24] identified by the review [21] did not report adverse events. Common adverse effects with oral corticosteroids include nausea, anxiety, acne, menstrual irregularities, insomnia, headaches, and mood swings. More serious adverse reactions include peptic ulcer, corticosteroid psychosis, osteoporosis, and adrenal insufficiency. [25]

Systemic corticosteroids versus local corticosteroid injection:
See harms of corticosteroids (local injection), p 3 .

Systemic corticosteroids versus NSAIDs:
The RCT reported no major adverse effects. [22] However, nausea (3/23 [13%] with prednisolone *v* 3/18 [17%] with tenoxicam) and epigastric pain (2/23 [9%] with prednisolone *v* 3/18 [17%] with tenoxicam; P values not reported) were less common with oral prednisolone than with tenoxicam.

Systemic corticosteroids versus diuretics:
See harms of diuretics, p 7 .

Systemic corticosteroids versus splints:
The RCT found that two people in the wrist splint group complained of discomfort and swelling of the hand and wrist. [23] However, discomfort improved with continued and correct use of the splint. No adverse effects were reported by those taking oral corticosteroids.

Comment: **Clinical guide:**
Long-term corticosteroid use can be associated with some, as yet unquantified, risks.

OPTION DIURETICS

Symptom severity
Compared with placebo We don't know whether diuretics are more effective at improving symptoms of CTS at 4 weeks and 6 months (low-quality evidence).

Compared with NSAIDs Diuretics seem equally effective at improving symptoms of CTS at 4 weeks (moderate-quality evidence).

Compared with systemic corticosteroids Diuretics seem less effective at improving symptoms of CTS at 4 weeks (moderate-quality evidence).

For GRADE evaluation of interventions for carpal tunnel syndrome, see table, p 27 .

Benefits:

Diuretics versus placebo:
We found one systematic review (search date 2002; 2 RCTs; 139 people with CTS) [21] comparing diuretics versus placebo. The review did not pool data because of clinical heterogeneity among interventions, outcome measures, or participants. [21] The first RCT (91 people) identified by the review compared oral prednisolone (20 mg/day for 2 weeks followed by 10 mg/day for another 2 weeks; 26 people), an oral slow-release NSAID (tenoxicam 20 mg/day; 22 people), an oral diuretic (trichlormethiazide 2 mg/day; 20 people), and placebo (23 people). [22] It found no significant difference between trichlormethiazide (16 people) and placebo (16 people) in mean Global Symptom Score (GSS) after 4 weeks (21.6 with diuretics *v* 20.8 with placebo; mean difference +0.80, 95% CI –3.67 to +5.27). [21]

The second RCT (48 people) [26] included in the review [21] compared bendroflumethiazide 5 mg daily for 4 weeks versus placebo. The systematic review found no significant difference between bendroflumethiazide and placebo in the proportion of people with symptom improvement after 4 weeks of treatment (19/41 [46%] with bendroflumethiazide *v* 20/40 [50%] with placebo; RR 0.93, 95% CI 0.59 to 1.46). [21] It also found no significant difference in symptom improvement at 6 months (14/19 [74%] with bendroflumethiazide *v* 15/20 [75%] with placebo; RR 0.98, 95% CI 0.68 to 1.42). The RCT used a numerical score from 0 to 5 to assess the degree of improvement in reported symptoms (0 = no improvement at all; 5 = full recovery). [26]

Diuretics versus NSAIDs:
We found one systematic review (search date 2002), [21] which identified one RCT (91 people) [22] comparing oral prednisolone (20 mg/day for 2 weeks followed by 10 mg/day for another 2 weeks; 26 people), an oral slow-release NSAID (tenoxicam 20 mg/day; 22 people), an oral diuretic (trichlormethiazide 2 mg/day; 20 people), and placebo (23 people). It found no significant difference in GSS between trichlormethiazide and tenoxicam at 4 weeks (21.6 with diuretics *v* 24 with NSAIDs; mean difference –2.40, 95% CI –7.84 to +3.04). [21]

Diuretics versus systemic corticosteroids:
We found one systematic review (search date 2002), [21] which identified one RCT (91 people) [22] comparing oral prednisolone (20 mg/day for 2 weeks followed by 10 mg/day for another 2 weeks; 26 people), an oral slow-release NSAID (tenoxicam 20 mg/day; 22 people), an oral diuretic (trichlormethiazide 2 mg/day; 20 people), and placebo (23 people) (see comment on corticosteroids [systemic], p 5). It found that prednisolone significantly improved GSS at 4 weeks compared with trichlormethiazide (21.6 with diuretics *v* 10 with systemic corticosteroids; mean difference 11.60, 95% CI 7.25 to 15.95). [21]

Harms:

Diuretics versus placebo:
The first RCT found no difference in rates of epigastric pain between trichlormethiazide and placebo (2/16 [13%] with trichlormethiazide *v* 2/16 [13%] with placebo). [22]

Diuretics versus NSAIDs:
The RCT found that nausea and epigastric pain were less common with trichlormethiazide than with tenoxicam (nausea: 0/16 [0%] people with trichlormethiazide *v* 3/18 [17%] with tenoxicam; epigastric pain: 2/16 [13%] with trichlormethiazide *v* 3/18 [17%] with tenoxicam; P values not reported). [22]

Diuretics versus systemic corticosteroids:
The RCT found that nausea was less common with trichlormethiazide than with prednisolone (0/16 [0%] with trichlormethiazide *v* 3/23 [13%] with prednisolone), although epigastric pain was more

common with trichlormethiazide than with prednisolone (2/16 [13%] with trichlormethiazide *v* 2/23 [9%] with prednisolone; P values not reported). [22]

Comment: **Clinical guide:**
There is weak evidence that diuretics might be effective in people with CTS and fluid retention.

OPTION NSAIDS

Symptom severity
Compared with placebo NSAIDs seem no more effective at improving symptoms of CTS at 4 weeks (moderate-quality evidence).

Compared with systemic corticosteroids NSAIDs seem less effective at improving symptoms of CTS at 4 weeks (moderate-quality evidence).

Compared with diuretics NSAIDs seem equally effective at improving symptoms of CTS at 4 weeks (moderate-quality evidence).

For GRADE evaluation of interventions for carpal tunnel syndrome, see table, p 27 .

Benefits: **NSAIDs versus placebo:**
We found one systematic review (search date 2002), [21] which identified one RCT [22] comparing oral prednisolone (20 mg/day for 2 weeks followed by 10 mg/day for another 2 weeks; 26 people), an oral slow-release NSAID (tenoxicam 20 mg/day; 22 people), an oral diuretic (trichlormethiazide 2 mg/day; 20 people), and placebo (23 people). It found no significant difference between tenoxicam (18 people) and placebo (16 people) in mean Global Symptom Score (GSS) after 4 weeks (24 with NSAIDs *v* 20.8 with placebo; mean difference +3.2, 95% CI –1.7 to +8.1). [21]

NSAIDs versus systemic corticosteroids:
See benefits of corticosteroids (systemic), p 5 .

NSAIDs versus diuretics:
See benefits of diuretics, p 7 .

Harms: **NSAIDs versus placebo:**
The RCT reported no major adverse effects. [22] The RCT found that tenoxicam increased the proportion of people with nausea and epigastric pain compared with placebo (nausea: 3/18 [17%] with tenoxicam *v* 1/16 [6%] with placebo; epigastric pain: 3/18 [17%] with tenoxicam *v* 2/16 [12%] with placebo; P values not reported). [22]

NSAIDs versus systemic corticosteroids:
See harms of corticosteroids (systemic), p 5 .

NSAIDs versus diuretics:
See harms of diuretics, p 7 .

Comment: **Clinical guide:**
NSAIDs can be clinically useful if there seems to be a substantial degree of tendonitis or tenosynovitis associated with CTS.

OPTION PYRIDOXINE

Symptom severity
Compared with placebo or no treatment Pyridoxine may be no more effective at improving symptoms of CTS at 12 weeks (low-quality evidence).

For GRADE evaluation of interventions for carpal tunnel syndrome, see table, p 27 .

Benefits: **Pyridoxine versus placebo:**
We found one systematic review (search date 2002), [21] which identified two RCTs comparing pyridoxine versus placebo. The review did not pool data, because different outcome measures were used in the RCTs. The first RCT [27] identified by the review [21] included only 15 people and does not meet *Clinical Evidence* reporting criteria; therefore, this RCT will not be reported further here. The second RCT (35 people) [28] identified by the review [21] compared oral pyridoxine 200 mg daily versus placebo for 12 weeks. The systematic review found no significant difference at 12 weeks between pyridoxine and placebo in nocturnal discomfort, finger swelling, movement discomfort, or hand co-ordination (nocturnal discomfort: 1.9 with pyridoxine *v* 2.4 with placebo; mean dif-

ference [MD] –0.50, 95% CI –1.37 to +0.37; finger swelling: 1.3 with pyridoxine *v* 2.3 with placebo; MD –1.00, 95% CI –1.90 to –0.10; movement discomfort: 1.7 with pyridoxine *v* 2.1 with placebo; MD –1.00, 95% CI –1.94 to –0.06; hand co-ordination: 1.2 with pyridoxine *v* 1.8 with placebo; MD –0.60, 95% CI –1.57 to +0.37). [21] The RCT used an unvalidated 4-point questionnaire with discrete numerical scoring of symptom severity (0 = no symptoms; 4 = severe symptoms) to assess these outcomes. [28]

Harms:

Pyridoxine versus placebo:
The systematic review [21] and the second RCT [28] did not report on harms. Common adverse reactions (that can be associated with pyridoxine even at doses of 200–500 mg/day) include numbness, paraesthesia, and an unsteady gait. [25]

Comment: None.

QUESTION What are the effects of non-drug treatments for carpal tunnel syndrome?

OPTION ACUPUNCTURE

We found no clinically important results from RCTs about the effects of acupuncture in the treatment of carpal tunnel syndrome.

For GRADE evaluation of interventions for carpal tunnel syndrome, **see table, p 27 .**

Benefits: We found no systematic reviews or RCTs on acupuncture in the treatment of CTS.

Harms: We found no RCTs.

Comment: None.

OPTION MASSAGE THERAPY

We found no clinically important results from RCTs about the effects of massage therapy in the treatment of carpal tunnel syndrome.

For GRADE evaluation of interventions for carpal tunnel syndrome, **see table, p 27 .**

Benefits: We found no systematic reviews or RCTs on the effects of massage therapy in the treatment of CTS.

Harms: We found no RCTs.

Comment: None.

OPTION NERVE AND/OR TENDON GLIDING EXERCISES

Symptom severity
Compared with wrist splints alone Nerve or tendon gliding exercises plus splints may be no more effective at improving symptoms of CTS (very low-quality evidence).

Hand function
Compared with wrist splints alone Nerve or tendon gliding exercises plus splints may be no more effective at improving hand function scores (very low-quality evidence).

For GRADE evaluation of interventions for carpal tunnel syndrome, **see table, p 27 .**

Benefits:

Nerve and/or tendon gliding exercises versus placebo:
We found no RCTs.

Nerve and/or tendon gliding exercises plus splinting versus splinting alone:
We found one systematic review (search date 2008) [29] and one subsequent RCT. [30] The systematic review identified six RCTs, but did not perform meta-analyses because of heterogeneity among trials (neural gliding exercise prescription, follow-up periods, and comparison groups). Three trials identified by the systematic review do not meet *Clinical Evidence* reporting criteria (2 RCTs had fewer than 10 people per study arm, and 1 trial was not randomised), and so they are not reported further here.

The first RCT (28 people; 36 wrists) [31] identified by the review [29] compared nerve gliding plus tendon gliding exercises plus a custom-made neutral-angle wrist splint versus a wrist splint alone. The nerve and tendon gliding exercises were undertaken five times daily for 4 weeks, and people were instructed to wear the neutral-angle wrist splints all night and during the day as much as possible for 4 weeks. The RCT found no significant difference between nerve and tendon gliding exercises plus neutral-angle wrist splint and neutral-angle wrist splint alone in mean Symptom Severity Scale (SSS) score at 8 weeks (18.2 with splint plus exercises *v* 21.88 with splint alone; P = 0.2) or mean Functional Status Scale (FSS) score at 8 weeks (14.5 with splint plus exercises *v* 15.5 with splint alone; P = 0.5). [31] The RCT found that exercise significantly improved pinch strength, measured using a Martin vigorimeter, at 8 weeks compared with wrist splint alone (35.27 with wrist splint plus exercises *v* 30.0 with wrist splint alone; P = 0.026). However, it found no significant difference in grip strength (measured using a Martin vigorimeter), proportion of hands with positive Phalen's sign, or proportion of hands with positive Tinel's sign at 8 weeks (grip strength: 54.94 with wrist splint plus exercises *v* 49.88 with wrist splint alone; P = 0.14; proportion of hands with positive Phalen's sign: 5/14 [27%] with wrist splint plus exercises *v* 8/14 [44%] with wrist splint alone; P = 0.23; proportion of hands with positive Tinel's sign: 6/14 [33%] with wrist splint plus exercises *v* 8/14 [44%] with wrist splint alone; P = 0.83).

The second RCT (26 people with early-stage or middle-stage CTS; 35 hands) [32] identified by the review [29] compared nerve gliding exercises (10 repetitions five times daily) plus neutral splint plus a patient training programme for modifying functional activities versus neutral splint plus the same patient training programme for 10 weeks. The splints were worn day and night for the first 6 weeks, and only at night time during the subsequent 4 weeks. The RCT found no significant difference between exercise and no exercise in pain, pinch strength, and light-touch deep-pressure sense at 12 weeks (pain [measured by visual analogue scale, 0 = no pain, 10 = severe pain]: 1.0 with exercises *v* 1.6 with no exercises; mean pinch strength [measured using the Jamar pinch meter]: 5.4 kg with exercises *v* 4.9 kg with no exercises; light-touch deep-pressure sense at 12 weeks [measured by Semmes-Weinstein pressure aesthesiometer]; 2.9 mm with exercises *v* 2.8 mm with no exercises; P greater than 0.5 for all outcomes listed). The RCT found that exercises significantly improved grip strength at 12 weeks compared with no exercises (mean grip strength [measured using a Jamar hand dynamometer]: 22.0 kg with exercises *v* 21.7 kg with no exercises; P less than 0.05). However, multiple statistical analyses were performed without a correction factor for multiple testing; if a correction factor had been used, the results would probably not have been significant. The RCT found that exercises increased the proportion of people with negative Tinel's test and negative Phalen's test at 12 weeks compared with no exercises, but significance was not assessed (proportion of people with negative Tinel's test: 9/19 [47%] with exercises *v* 4/16 [25%] with no exercises; proportion of people with negative Phalen's test: 1/19 [5%] with exercises *v* 0/16 [0%] with no exercises; P values not reported).

The third RCT (61 people with CTS) [33] identified by the systematic review [29] compared four interventions: nerve and tendon gliding exercises plus neutral-angle wrist splint (16 people), neutral-angle wrist splint (17 people), nerve and tendon gliding exercises plus wrist cock-up splint (wrist splinting in 20° extension; 16 people), and wrist cock-up splint (12 people). All groups were instructed to wear the splints during sleep for 4 weeks, and the exercise groups were instructed to perform exercises three to five times daily for 4 weeks. All groups could continue wearing the splints and performing the exercises as needed to manage symptoms after the 4 weeks. The RCT performed a complex ANOVA analysis, but it did not report direct statistical analyses between any two individual groups. The RCT assessed three main factors in a factorial design (splint, exercise, and time), and found that nerve and tendon gliding exercises had no effect on CTS Symptom Severity Scale (CTS SSS), CTS Functional Status Scale (CTS FSS), tip pinch strength, or palmar pinch strength (at baseline, 4 weeks, and 8 weeks, absolute numbers and statistical analyses not reported). The RCT reported several limitations: about 41% of participants had been treated previously with splint or anti-inflammatory medications; 8% of participants received anti-inflammatory medication and 18% of participants received an injection during the study period; 67% of participants had symptoms for more than 6 months; and the administrator of treatment and outcome assessor (1 person) was not blinded to treatment allocation.

The subsequent RCT (61 people with CTS randomised; 60 people in the analysis) compared neurodynamic mobilisation exercise with a median nerve bias (10 repetitions 3–5 times daily) plus standard care (patient education, neutral splinting during heavy activity and during the night, and tendon gliding exercises) versus standard care alone for 6 months. [30] The RCT performed four separate MANCOVAs to assess whether there were any differences in four independent variables over time by intervention received. The four variables were the Disabilities of the Arm, Shoulder, and Hand (DASH) Questionnaire (a 30-item, self-report questionnaire to measure physical function and symptoms), the Brigham Women's Hospital Carpal Tunnel Specific Questionnaire (CTSQ) Symptom Severity Scale (CTSQ SSS; an 11-item questionnaire to measure symptoms), the CTSQ Functional Status Scale (CTSQ FSS; an 8-item questionnaire to measure function), and elbow

extension range of motion during an upper limb median nerve tension test. The RCT found no time-by-intervention interactions for DASH, CTSQ SSS, and elbow extension (DASH; P = 0.164; CTSQ SSS: P = 0.080; elbow extension: P = 0.366; results presented graphically). The RCT found a significant time-by-intervention interaction in the CTSQ FSS (P = 0.016; results presented graphically), but the authors of the RCT note that this result may have been because of significantly higher compliance in the nerve gliding exercise plus standard care group than the standard care alone group at 6 months (P = 0.01; further results not reported). The authors of the RCT commented that the study may have been underpowered to find a difference between groups because the follow-up rate at 6 months was only 48%.

Harms:

Nerve and/or tendon gliding exercises versus placebo:
We found no RCTs.

Nerve and/or tendon gliding exercises plus splinting versus splinting alone:
The three RCTs [31] [32] [33] identified by the systematic review [29] and the subsequent RCT [30] gave no information about adverse events.

Comment:

Clinical guide:
Most nerve and tendon gliding exercises typically involve some degree of stretching of the median nerve, which could exacerbate symptoms of CTS.

OPTION THERAPEUTIC ULTRASOUND

Symptom severity
Compared with placebo We don't know whether therapeutic ultrasound is more effective at improving symptoms at 6 months (very low-quality evidence).

For GRADE evaluation of interventions for carpal tunnel syndrome, **see table, p 27 .**

Benefits:

We found one systematic review (search date 2002). [21]

Therapeutic ultrasound versus placebo:
The systematic review identified two RCTs (88 people with CTS) comparing therapeutic ultrasound versus placebo. [21] One RCT identified by the review [21] reported outcomes only at 2 weeks and does not meet *Clinical Evidence* reporting criteria; therefore, this RCT will not be reported further here.

The other RCT [34] identified by the review [21] (45 people; 90 wrists) compared ultrasound (15 minutes, five times weekly for 2 weeks followed by twice weekly for 5 weeks, at an intensity of 1.0 W/cm^2) versus placebo. The dominant wrist was randomly allocated to ultrasound or placebo, and the contralateral wrist was allocated to the other treatment. [34] It found that ultrasound treatment significantly increased the proportion of wrists with "satisfactory improvement" or "complete remission" of symptoms at 6 months (22/30 [73%] wrists with ultrasound *v* 6/30 [20%] wrists with placebo; RR 3.7, 95% CI 1.7 to 7.7; NNT 2, 95% CI 2 to 4). [34] However, these results should be interpreted with caution because 15/45 (33%) people did not complete the trial, and analysis of data was not by intention to treat. [34] The RCT used "satisfactory improvement" and "complete remission" as outcome measures, although these terms were not clearly defined.

High- versus low-intensity ultrasound:
The systematic review [21] identified one RCT that compared high- versus low-intensity ultrasound. However, the RCT included fewer than 20 people and does not meet *Clinical Evidence* reporting criteria; therefore, this RCT will not be reported further here.

Harms:

Therapeutic ultrasound versus placebo:
The first RCT included in the review reported that there were no adverse effects with ultrasound. [34]

High- versus low-intensity ultrasound:
We found no RCTs that met *Clinical Evidence* reporting criteria.

Comment:

Clinical guide:
Ultrasound is either used alone or combined with nerve and tendon gliding exercises. There are many different types, intensities, and durations of ultrasound treatment (similar to the variation in different glide exercises), which makes evaluation of its effectiveness difficult.

OPTION WRIST SPLINTS

Symptom severity

Compared with no treatment Wrist splints worn at night time seem more effective at improving symptoms of CTS after 4 weeks (moderate-quality evidence).

Compared with open surgery Wrist splints may be less effective at improving symptoms of CTS after 3 to 18 months (low-quality evidence).

Compared with systemic corticosteroids We don't know whether splints are more effective at improving symptoms of CTS at 3 months (low-quality evidence).

Compared with nocturnal use alone Full-time use of a neutral wrist splint may be no more effective at reducing symptoms at 6 weeks (low-quality evidence).

Compared with cock-up splint We don't know whether neutral-angle splint is more effective at improving symptoms of CTS (very low-quality evidence).

Hand function

Compared with systemic corticosteroids Splints may be less effective at improving hand function in people with CTS at 3 months (low-quality evidence).

For GRADE evaluation of interventions for carpal tunnel syndrome, see table, p 27 .

Benefits:

Wrist splints versus no treatment:

We found one systematic review (search date 2000), [21] which identified one RCT (83 people) [35] comparing a nocturnal hand brace worn for 4 weeks versus no treatment. The RCT found that the hand brace significantly improved symptoms at 4 weeks compared with no treatment. [35] Symptoms were assessed using the symptom domain of the Boston Carpal Tunnel Questionnaire [36] (BCTS SYMPT; BCTQ symptom severity score [improvement from baseline] at 4 weeks: 1.54 [1.21] with hand brace *v* 1.48 [0.41] with no treatment; P less than 0.001). [35]

Wrist splints versus surgery:

See benefits of surgery, p 16

Wrist splints versus systemic corticosteroids:

See benefits of corticosteroids (systemic), p 5 .

Different wrist splinting regimens compared with each other:

We found one systematic review (search date 2002) [21] and one subsequent RCT. [33] The review identified two RCTs comparing different wrist splinting regimens versus each other, but did not pool data because of clinical heterogeneity among interventions, outcome measures, or participants. [21] One RCT identified by the review [21] reported outcomes only at 2 weeks and does not meet *Clinical Evidence* reporting criteria; therefore, this RCT will not be reported further here.

The second RCT identified by the review (24 people with CTS) compared full-time (day and night) wear of neutral-angle wrist splints versus night-time only wear, and used a validated numerical scale (11 items, each measured on a scale of 1–5, where 1 = least severe and 5 = most severe) to assess changes in symptom severity. It found no significant difference between groups at 6 weeks (mean symptom severity score [improvement from baseline] at 6 weeks: 2.09 [–0.41] with full-time splint *v* 2.30 [–0.59] with night-time splint; P = 0.53). [37] The use of a night-time splint was complete or nearly complete in 85% of people allocated to night-time splinting only, but 23% reported limited additional daytime use. Complete or nearly complete daytime wear was reported by only 27% of people allocated to full-time wear. More men than women were included in the trial than would have been expected from the usual sex distribution of CTS.

The subsequent RCT (61 people with CTS randomised; 60 people analysed, most with symptoms over 6 months' duration; 41% previously treated with splint or anti-inflammatory) compared four interventions: neutral-angle splint (17 people), neutral-angle splint with nerve gliding exercises (16 people), wrist cock-up splint (wrist splinting in 20° extension; 12 people), versus wrist cock-up splint with nerve gliding exercises (16 people). [33] All groups were instructed to wear the splints during sleep for 4 weeks, and the exercise groups were instructed to perform exercises three to five times daily for 4 weeks. All groups could continue wearing the splints and performing the exercises as needed to manage symptoms after the 4 weeks. The RCT performed a complex ANOVA analysis among all four groups, but it did not report direct statistical analyses between any two individual groups. The RCT reported absolute symptom scores for people wearing different types of splint; however, it is unclear whether people performing exercises were included in the scores for the

neutral-angle splint and wrist cock-up splint groups. The RCT found that people wearing the neutral-angle splint had greater improvements in symptoms than people wearing the wrist cock-up splint (mean CTS Symptom Severity Scale score [a higher score denotes worse symptoms]: 2.0 with neutral splint *v* 2.5 with wrist cock-up splint; time frame unclear, absolute numbers in analysis not reported, statistical analyses between groups not reported). The RCT reported that some participants received anti-inflammatory medication (8%) or an injection (18%) during the study period, which may have affected the results, and that the administrator of treatment and outcome assessor (the same person) was not blinded to treatment allocation.

Harms:

Wrist splints versus no treatment:
In the RCT comparing nocturnal hand brace with no treatment, four people in the hand brace group experienced transient paraesthesiae after the hand brace was removed. [35]

Wrist splints versus surgery:
See harms of surgery, p 16

Wrist splints versus systemic corticosteroids:
See harms of corticosteroids (systemic), p 5 .

Different wrist splinting regimens compared with each other:
The RCTs gave no information about adverse effects. [37] [33]

Comment:

We identified one study comparing corticosteroid injection versus night-time splint versus physiotherapy (ultrasound or TENS), which will be considered for inclusion once translated. [20]

Clinical guide:
There is limited evidence that wearing a splint full time (i.e., 24 hours a day) versus just night-time use is beneficial. There seems no difference in effectiveness between splints that hold the joint in a neutral position or those holding it at an angle of approximately 20°.

QUESTION What are the effects of surgical treatments for carpal tunnel syndrome?

OPTION ENDOSCOPIC CARPAL TUNNEL RELEASE VERSUS OPEN CARPAL TUNNEL RELEASE

Symptom severity
Endoscopic compared with open carpal tunnel release Endoscopic carpal tunnel release seems equally effective at improving symptoms in people with CTS in the short or long term (moderate-quality evidence).

Hand function
Endoscopic compared with open carpal tunnel release Endoscopic carpal tunnel release seems equally effective at improving hand function in people with CTS in the short or long term (moderate-quality evidence).

Time to return to work
Endoscopic compared with open carpal tunnel release Endoscopic surgery may be more effective at reducing time to return to work in people with CTS (moderate-quality evidence).

Adverse effects
Adverse effects of carpal tunnel surgeries are usually minor but can include nerve injuries, haemorrhage and infection, persistent pain (in wrist or over scar), and persistence/recurrence of symptoms of CTS. Endoscopic release is more resource-intensive than open carpal tunnel release, and requires a higher degree of surgical skill.

For GRADE evaluation of interventions for carpal tunnel syndrome, see table, p 27 .

Benefits:

Endoscopic versus open carpal tunnel release:
We found two systematic reviews (search date 2001/2002 [38] and search date 2006) [39] and one subsequent RCT. [40] The first systematic review compared endoscopic carpal tunnel release (any technique) versus open carpal tunnel release (any technique). It identified 12 RCTs of variable quality and pooled data. [38] The second systematic review compared any surgical technique versus any other surgical technique in people with CTS. [39] It identified 19 RCTs comparing endoscopic versus standard open carpal tunnel release or open carpal tunnel release with a modified incision. The second review pooled data for some RCTs for some outcomes. The two systematic reviews had 10 RCTs in common. The subsequent RCT compared endoscopic versus standard open carpal tunnel release. [40]

Short-term outcomes (3 months or less):
The first systematic review found no significant difference in pain outcomes at 12 weeks between endoscopic and open surgery (see table 1, p 23). [38] However, it found that endoscopic surgery

significantly improved both grip and pinch strength at 12 weeks compared with open carpal tunnel release (see table 1, p 23). [38] Particular caution should be applied to the interpretation of the results for grip strength, because of significant heterogeneity between trials (see comment below).

The second systematic review identified 11 RCTs assessing short-term outcomes of endoscopic versus standard open carpal tunnel release. [39] It performed meta-analyses of three RCTs and found no significant difference in symptom severity between endoscopic and standard open carpal tunnel release at 3 months or less, and found that open carpal tunnel release significantly worsened function at 3 months or less compared with endoscopic carpal tunnel release (see table 1, p 23). However the authors of the review noted significant statistical heterogeneity for these two outcomes (see table 1, p 23), which is possibly attributable to one RCT. [39] Of the remaining eight RCTs assessing short-term outcomes, seven found no significant differences between endoscopic and standard open carpal tunnel release in short-term symptoms, [41] [42] [43] [44] [45] [46] (data for one RCT extracted from the systematic review [39]) and one did not report significance (see table 1, p 23). [47]

The second systematic review identified two RCTs assessing short-term outcomes of endoscopic versus open carpal tunnel release with a modified incision; it did not perform a meta-analysis. [39] One RCT did not meet *Clinical Evidence* criteria (only 10 people were included), and therefore it is not reported further here. The other RCT found that open carpal tunnel release with a modified incision significantly improved wound pain at 4 weeks, and radial/ulnar pillar pain at 8 weeks, compared with endoscopic carpal tunnel release. However, it found no significant difference between groups in wound pain at 8 weeks (see table 1, p 23). [48]

The subsequent RCT found no significant difference in 2-point discrimination (from baseline to post-operation; time of postoperative assessment not clear) between endoscopic and standard open carpal tunnel release (see table 1, p 23). [40] However, it found that endoscopic carpal tunnel release significantly reduced scar tenderness at the most "significant point" (type of measurement and time frame not reported) compared with open carpal tunnel release (see table 1, p 23).

Long-term outcomes (more than 3 months):
The first systematic review did not assess long-term outcomes of endoscopic versus open carpal tunnel release. [38]

The second systematic review identified eight RCTs assessing long-term outcomes of endoscopic versus standard open carpal tunnel release. [39] It performed meta-analyses of two RCTs and found no significant difference in symptom severity or function at more than 3 months between endoscopic and standard open carpal tunnel release (see table 1, p 23). Of the remaining six RCTs [42] [43] [44] [45] [47] (data for one RCT extracted from the systematic review [39]) assessing long-term outcomes, the review reported that all six found no significant difference between endoscopic and standard open carpal tunnel release in long-term symptoms (see table 1, p 23). [39]

An extended follow-up (126 people) [49] for one of the original RCTs comparing endoscopic versus standard open carpal tunnel release (128 people) [50] found that symptom severity and function, as measured by the Boston Carpal Tunnel Questionnaire, [36] were similar in both the endoscopic and open carpal tunnel release groups at 5 years (symptom severity: 1.45 with endoscopic *v* 1.42 with open; significance between groups not reported; functional status: 1.30 with endoscopic *v* 1.29 with open; significance between groups not reported).

The second systematic review identified one RCT that assessed long-term outcomes of endoscopic carpal tunnel release versus open carpal tunnel release with a modified incision. It found no significant difference between the two groups in overall symptom improvement (see table 1, p 23). [39]

The subsequent RCT found that there was no significant difference in patient satisfaction at approximately 2 years' follow-up (18–48 months) between endoscopic and standard open carpal tunnel release. [40]

Time to return to work or activities of daily living:
The first systematic review found no significant difference in time taken to return to work between endoscopic and open surgery (see table 1, p 23). [38]

The second systematic review identified 14 RCTs assessing return to work or resumption of activities of daily living (ADL) for release versus standard open carpal tunnel release. [39] It performed a meta-analysis of three RCTs [46] [50] [51] and found that people receiving standard open carpal tunnel release took significantly longer to return to work and resume ADL than people receiving endoscopic carpal tunnel release (see table 1, p 23). Of the remaining 11 RCTs assessing time to return to work or resumption of ADL, six RCTs (1 RCT reported in 2 publications) found that

endoscopic carpal tunnel release significantly decreased the time to return to work or resume ADL compared with standard open carpal tunnel release; [52] [53] [54] [41] [43] [47] [55] one RCT found that open carpal tunnel release significantly decreased the time to return to work or resume ADL compared with endoscopic carpal tunnel release; [42] and four RCTs [56] [57] [45] (data for 1 RCT extracted from the systematic review [39]) found no significant differences between endoscopic and standard open carpal tunnel release in long-term symptoms (see table 1, p 23).

The second systematic review identified no RCTs assessing return to work or ADL for the comparison of endoscopic versus open carpal tunnel release with a modified incision. [39]

The subsequent RCT found that endoscopic carpal tunnel release significantly reduced the time to return to work compared with standard open carpal tunnel release (see table 1, p 23). [40]

Harms:

Endoscopic versus open carpal tunnel release:
The first systematic review found that reversible nerve injury was significantly more common (by about 3 times) in the endoscopic group (6 RCTs, pooled OR 0.336, 95% CI 0.117 to 0.908; homogeneity P = 0.975). [38] However, it found significantly more scar tenderness with open than endoscopic surgery (pooled OR 3.78, 95% CI 2.16 to 6.59; homogeneity P = 0.0116). [38]

The second systematic review identified 15 RCTs reporting on complications of endoscopic versus standard open carpal tunnel release. [39] It found no significant difference in need for repeated surgery between endoscopic and standard open carpal tunnel release (6 RCTs, 883 people: 12/513 [2%] with endoscopic carpal tunnel release *v* 5/370 [1%] with standard open carpal tunnel release; RR 1.24, 95% CI 0.50 to 3.07). The second review also identified one RCT comparing endoscopic carpal tunnel release versus open carpal tunnel release with a modified incision, assessing repeat surgery. The review found that repeat surgery was significantly less common with endoscopic carpal tunnel release than open carpal tunnel release with a modified incision (2/128 [2%] with endoscopic *v* 6/65 [9%] with modified open; RR 0.17, 95% CI 0.04 to 0.82). The review reported that no major complications occurred resulting in permanent damage or major impairments, and stated that "It seems that endoscopic carpal tunnel release gives more transient nerve problems (for example neurapraxia, numbness, paraesthesiae) and open carpal tunnel release more wound problems (for example, infection, hypertrophic scarring, scar tenderness)."

Harms resulting from endoscopic and open carpal tunnel release vary between RCTs, although rates of complications for both procedures are generally low. [58] [53] [47] [41] [43] [56] [52] [59]

The subsequent RCT reported that no neurovascular or infection complications occurred as a result of endoscopic or open carpal tunnel release. [40] It found that scar tenderness (type of measurement not reported) at "the most significant point" (time frame not clear) was significantly improved with endoscopic compared with standard open carpal tunnel release (36% with endoscopic *v* 65% with open; absolute numbers not reported; P less than 0.05). Surgery was repeated in 3/30 (10%) people with endoscopic carpal tunnel release versus 0/32 (0%) people with standard open carpal tunnel release; significance not assessed.

Comment:

The lack of significant homogeneity between trials using pinch strength as an outcome could not be explained by differences in baseline characteristics, surgical technique, definitions of outcomes, or methods. This could suggest the existence of an undefined subgroup of people who might benefit from, or conversely be harmed by, endoscopic release surgery. Endoscopic release techniques vary between RCTs, which might account for some of the variation seen in outcomes. [60] [39]

Clinical guide:
Endoscopic surgery is more resource-intensive and demands a higher surgical skill level than the open technique.

OPTION SURGERY VERSUS NO TREATMENT

We found no clinically important results from RCTs about the effects of surgery compared with no treatment or placebo.

For GRADE evaluation of interventions for carpal tunnel syndrome, see table, p 27 .

Benefits:

Surgery versus no treatment:
We found no RCTs comparing surgery versus placebo or no treatment.

Harms:

Surgery versus no treatment:
We found no RCTs.

Comment: **Clinical guide:**
There is no consensus as to the optimal timing of when to operate on the carpal tunnel. Most clinicians believe that those who have not benefited from conservative management (e.g., a trial of wrist splints or corticosteroid injection) should be considered for surgery. Electrodiagnostic testing (electromyelogram) can identify people with severe CTS who should probably be referred for surgery, and those in the mild and moderate categories who can be given a trial of conservative treatment(s). People with predisposing conditions, such as diabetes or previous wrist fracture, should possibly be managed more aggressively, with earlier referral for surgery.

OPTION SURGERY VERSUS WRIST SPLINT

Symptom severity
Compared with wrist splints Surgery may be more effective at reducing symptoms of carpal tunnel syndrome after 3 to 18 months (low-quality evidence).

For GRADE evaluation of interventions for carpal tunnel syndrome, see table, p 27 .

Benefits: **Surgery versus wrist splint:**
We found one systematic review (search date 2008) comparing any type of surgery with any non-surgical intervention. [61] The review identified two RCTs comparing surgery versus splints, and two RCTs comparing surgery versus local corticosteroid injection (see benefits of surgery versus local corticosteroid injection, p 16).

The systematic review found that surgery significantly improved clinical outcome at 1 year compared with splints (2 RCTs,198 people with carpal tunnel syndrome: 77/98 [79%] with surgery *v* 62/100 [62%] with splint; RR 1.27, 95% CI 1.05 to 1.53). [61] The review noted several methodological flaws in the first RCT, including that it was not blinded, there was no information on baseline clinical and electrophysiological status of the two groups, and the method of randomisation was not described.

The second RCT [62] identified by the systematic review [61] (176 people, including 143 women; duration of symptoms 16–104 weeks) also reported on clinical improvement at 3 and 18 months. The RCT compared open carpal tunnel surgery with wrist splinting for at least 6 months. It found that surgery significantly increased success rates (defined as "completely recovered" or "much improved" on a 6-point scale) compared with splinting at 3 and 18 months (3 months: 62/78 [80%] with surgery *v* 46/86 [54%] with splinting; P less than 0.001; 18 months: 61/68 [90%] with surgery *v* 59/79 [75%] with splinting; P = 0.02). By 18 months, 41% of the people allocated to splinting had had surgery. [62] This second RCT was larger, of much better quality, and had longer follow-up (up to 18 months) than the first smaller RCT identified by the review. [61]

Harms: **Surgery versus wrist splint:**
The first RCT identified by the review did not report on harms of treatment. [61] The second RCT [62] identified by the review [61] found that the proportion of people with adverse effects was higher in the surgery group than the splint group, but the difference was of borderline significance (58/87 [67%] with surgery *v* 46/89% [52%] with splinting; RR 1.29, 95% CI 1.00 to 1.66). [61] However, the systematic review noted that a number of adverse events reported in the non-surgical group were actually caused by surgery during follow-up. Adverse effects included painful or hypertrophic scar, wound haematoma and infection, stiffness, swelling or discomfort of the wrist, and reflex sympathetic dystrophy. The review did not describe major complications such as damage to a nerve. [61]

Comment: **Clinical guide:**
There is no consensus as to the optimal timing of when to operate on the carpal tunnel. Most clinicians believe that those who have not benefited from conservative management (e.g., a trial of wrist splints, or corticosteroid injection) should be considered for surgery. Electrodiagnostic testing (electromyelogram) can identify people with severe CTS who should probably be referred for surgery, and those in the mild and moderate categories who can be given a trial of conservative treatment(s). People with predisposing conditions, such as diabetes or previous wrist fracture, should possibly be managed more aggressively, with earlier referral for surgery.

OPTION SURGERY VERSUS LOCAL CORTICOSTEROID INJECTION

Symptom severity
Compared with local corticosteroid injection We don't know whether carpal tunnel release surgery is more effective at improving symptoms of CTS (low-quality evidence).

Hand function
Compared with local corticosteroid injection Carpal tunnel release surgery may be equally effective at improving hand function in people with CTS (moderate-quality evidence).

For GRADE evaluation of interventions for carpal tunnel syndrome, see table, p 27 .

Benefits:

Surgery versus local corticosteroid injection:
We found one systematic review (search date 2008) comparing any type of surgery with any non-surgical intervention. [61] The review identified two RCTs comparing surgery versus local corticosteroid injection and two RCTs comparing surgery versus splints (see benefits of surgery versus wrist splint, p 16). The systematic review did not perform a meta-analysis exclusively for the comparison of surgery versus local corticosteroid injection; therefore, we report the RCTs individually here.

The first RCT identified by the systematic review (101 people, 93 women; mean duration of symptoms 31–33 weeks) [63] [61] compared carpal tunnel release surgery (using a limited palmar incision technique) versus local corticosteroid injection (paramethasone 20 mg). The systematic review found that surgery was significantly less effective than local corticosteroid injection at improving nocturnal paraesthesia at 3 months (proportion of people with 70% improvement: 29/33 [88%] with injection *v* 21/36 [58%] with surgery; RR 0.66, 95% CI 0.49 to 0.90); however, it found no significant differences between the groups at 6 months (24/33 [73%] with injection *v* 25/36 [69%] with surgery; RR 0.95, 95% CI 0.71 to 1.29). [61]

The second RCT identified by the systematic review (50 people with CTS) [61] compared surgical decompression (via open technique under local anaesthesia) versus local corticosteroid injection (15 mg methylprednisolone). The RCT found that surgery significantly improved clinical outcome at 20 weeks compared with local corticosteroid injection (proportion of people with improvement by at least 50% in the Global Symptom Score: 24/15 [96%] with surgery *v* 11/25 [44%] with corticosteroid injection; RR 2.18, 95% CI 1.39 to 3.42). [61] However, the RCT found no significant difference between the groups in the proportion of people with improved grip strength at 20 weeks (as measured by a JAMAR hydraulic hand dynamometer: 12/25 [48%] with surgery *v* 17/25 [68%] with corticosteroid; RR 0.71, 95% CI 0.43 to 1.15). [61]

Harms:

Surgery versus local corticosteroid injection:
The first RCT [63] identified by the systematic review [61] found that the proportion of people with adverse effects in each group was similar in each group (8/56 [14%] with surgery *v* 8/49 [16%] with corticosteroid injection; P value not reported). Adverse events included local wrist pain at 2 weeks, which resolved within "days". Colles' fracture leading to withdrawal was reported in two people who received corticosteroid injection, and death from hepatocarcinoma at 13 months was reported in one person in the surgery group. [63]

The second RCT identified by the systematic review [61] found that surgery significantly increased the proportion of people with adverse events compared with corticosteroid injection (11/25 [44%] with surgery *v* 5/25 [20%] with corticosteroid injection; RR 1.38, 95% CI 1.08 to 1.76). [61] Adverse effects in the surgery group were wound haematoma (2 people) and mild to moderate wound pain (9 people), and in the corticosteroid injection group were cellulitis (1 person) and pain at the injection site (4 people). [61]

Comment:

Clinical guide:
There is no consensus as to the optimal timing of when to operate on the carpal tunnel. Most clinicians believe that those who have not benefited from conservative management (e.g., a trial of wrist splints, or corticosteroid injection) should be considered for surgery. Electrodiagnostic testing (electromyelogram) can identify people with severe CTS who should be referred for surgery, and those in the mild and moderate categories who can be given a trial of conservative treatment(s). People with predisposing conditions, such as diabetes or previous wrist fracture, should possibly be managed more aggressively, with earlier referral for surgery.

OPTION INTERNAL NEUROLYSIS IN CONJUNCTION WITH OPEN CARPAL TUNNEL RELEASE

Symptom severity
Compared with carpal tunnel release alone Internal neurolysis may not reduce symptoms of CTS when performed at open surgery (low-quality evidence).

For GRADE evaluation of interventions for carpal tunnel syndrome, see table, p 27 .

Benefits:

Internal neurolysis in conjunction with open carpal tunnel release:
We found one systematic review (search date 2006), which identified three RCTs comparing open carpal tunnel release alone versus open carpal tunnel release plus internal neurolysis. [39] The review did not perform meta-analysis because of the use of different outcome measures or different scales. The three RCTs found no significant difference between open carpal tunnel release alone and open carpal tunnel release plus internal neurolysis. [64] [65] [66]

The first RCT (59 people; 63 wrists) found no significant difference between treatments in the proportion of people reporting relief from all or most of their symptoms after 12 months (28/32 [88%] with open carpal tunnel release alone *v* 25/31 [81%] with open carpal tunnel release plus internal neurolysis; RR 1.1, 95% CI 0.9 to 1.3). [64]

The second RCT (48 people; 48 wrists) found no significant difference between treatments in the proportion of people who reported complete relief of symptoms after 6 months (23/24 [96%] with open carpal tunnel release alone *v* 23/24 [96%] with open carpal tunnel release plus internal neurolysis; RR 1.0, 95% CI 0.9 to 1.1). [65]

The third RCT (41 people; 47 wrists with severe CTS; see comment below) found no significant difference after 3 months between treatments in the proportion of wrists with a "good" (resolution of pain, improvement in sensory deficit, and no surgical complications) or "excellent" (resolution of pain, resolution of sensory deficit, and no surgical complications) clinical response (15/23 [65%] wrists with open carpal tunnel release alone *v* 16/24 [67%] wrists with open carpal tunnel release plus internal neurolysis; RR 1.0, 95% CI 0.6 to 1.5). [66]

Harms:

Internal neurolysis in conjunction with open carpal tunnel release:
The first RCT did not report on harms. [64] The second RCT stated that there were no complications attributable to internal neurolysis. [65] The third RCT found no significant difference between treatments in the proportion of wrists with persistent incisional pain, which was the most common complication reported in the trial (3/23 [13%] wrists with open carpal tunnel release alone *v* 4/24 [17%] wrists with open carpal tunnel release plus internal neurolysis; RR 0.8, 95% CI 0.2 to 3.1). [66] Other complications included 1/24 (4%) wrists with hand swelling and 1/24 (4%) wrists with adhesive capsulitis in the open carpal tunnel release plus internal neurolysis group and 1/23 (4%) wrists with causalgia in the open carpal tunnel release alone group.

Comment:

The terms "epineurectomy" and "neurolysis" are sometimes used interchangeably in the medical literature, and yet they might have been referring to different surgical procedures. This could result in considerable heterogeneity between studies, and calls into question the validity of combining the results in a meta-analysis. In this review we have included RCTs that specifically refer to "neurolysis".

QUESTION What are the effects of postoperative treatments for carpal tunnel syndrome?

OPTION WRIST SPLINTS AFTER CARPAL TUNNEL RELEASE SURGERY

Symptom improvement
Compared with no movement restriction Wrist splinting after surgery may be no more effective at improving symptoms (very low-quality evidence).

Hand function
Compared with no movement restriction Wrist splinting after surgery may be no more effective at improving grip strength (low-quality evidence).

Return to work
Compared with no movement restriction Wrist splinting after surgery seems less effective at reducing the time to return to work (moderate-quality evidence).

For GRADE evaluation of interventions for carpal tunnel syndrome, see table, p 27 .

Benefits:

Wrist splints after carpal tunnel release surgery versus unrestricted range of motion:
We found no systematic review, but we found three RCTs. [67] [68] [69] The first RCT (74 people; 82 wrists) compared rigid wrist splinting for 4 weeks after surgery versus no splinting plus advice to mobilise the affected wrist or wrists. [67] It found no significant difference between treatments in median grip strength at 6 months (as a percentage of median pre-operative grip strength: unsplinted 104%, 95% CI 94% to 115% *v* splinted 108%, 95% CI 100% to 116%; reported as not significant; P values not reported).

The second RCT (47 people; 51 wrists) compared rigid wrist splinting for 2 weeks after surgery versus no splinting. [68] It found no significant difference in the proportion of people who considered themselves "cured" at follow-up (12/26 [46%] with splinting *v* 8/17 [47%] with no splinting; RR 1.0, 95% CI 0.5 to 1.9). In the second RCT, although the term "cured" was used as an outcome measure, its meaning was not defined in the context of the trial, and the length of follow-up was not specified. It found that 7/47 (15%) people were lost to follow-up, but analysis of data was not by intention to treat. [68]

The third RCT (50 people; 50 wrists) compared rigid wrist splinting for 2 weeks after surgery versus no splinting. [69] It found that the average number of days taken to return to work was significantly lower in the unsplinted group (27 days with splinting *v* 17 days with no splinting; P = 0.005). [69]

Harms: **Wrist splints after carpal tunnel release surgery versus unrestricted range of motion:** The first RCT found no significant difference between treatments in the proportion of people reporting scar pain after 6 months (6/37 [16%] with splinting *v* 6/44 [14%] with no splinting; RR 1.2, 95% CI 0.4 to 3.4). [67] The second RCT reported complications for one person in the unsplinted group, who had persistent symptoms and required re-operation. [68] The third RCT found that splinting significantly increased pillar pain and scar tenderness at 1 month, but found no significant difference between treatments in pain at 3 or 6 months after surgery (pillar pain: P = 0.02; scar tenderness: P = 0.04; pain: data not reported). [69]

Comment: The RCTs were too small to exclude the possibility of a clinically important increase in the risk of some complications (e.g., transient ulnar nerve injury) with splinting compared with no splinting.

GLOSSARY

Adhesive capsulitis A condition in which the joint capsule becomes contracted and thickened, causing restriction in the range of movement.

American Academy of Neurology diagnostic criteria [3] The likelihood of carpal tunnel syndrome increases with the number of standard symptoms and provocative factors. Symptoms include dull aching discomfort in the hand, forearm, or upper arm; paraesthesia in the hand; weakness or clumsiness of the hand; dry skin, swelling, or colour changes in the hand; or occurrence of any of these symptoms in the distribution of the median nerve. Provocative factors include sleep, sustained arm or hand positions, or repetitive actions of the hand or wrist. Relieving factors include changes in hand posture and shaking the hand. Physical examination may be normal, or symptoms may be elicited by tapping or direct pressure over the median nerve at the wrist or with forced flexion or extension of the wrist. Physical signs include sensory loss in the median nerve distribution; weakness or atrophy in the thenar muscles; and dry skin on the thumb, index, or middle fingers. Electromyography and nerve conduction studies can confirm, but not exclude, the diagnosis of carpal tunnel syndrome.

Internal neurolysis Decompression within the nerve accomplished by performing an epineurotomy and then dividing the nerve into multiple fascicular groups. [66]

Nerve gliding exercises Exercise therapy directed at restoring and maximising excursion of the median nerve through the carpal tunnel. [71]

Phalen's test/sign Tingling in the median nerve distribution is induced by full flexion (or full extension for reverse Phalen) of the wrists for up to 60 seconds.

Pillar pain Pain at the radial or ulnar border of the carpal tunnel.

Tendon gliding exercises Exercise therapy directed at restoring and maximising excursion of the finger flexor tendons through the carpal tunnel. [71]

Boston Carpal Tunnel Questionnaire (BCTQ) A validated self-administered questionnaire evaluating two domains: BCTQ SYMPT assesses symptom severity using an 11-point scale, and BCTQ FUNCT assesses function using eight items that are each rated on a scale of 1 (best score) to 5 (worst score).

Disabilities of Arm Shoulder and Hand (DASH) functional index is a 30-item questionnaire designed to assess function in people with musculoskeletal disorders of the upper limb. Each item is scored from 1–5, and the total score is converted to a 1–100 scale.

Functional Status Scale (FSS) Measures eight items, including difficulty in writing, buttoning clothes, opening jars, holding a book, gripping a telephone handle, household chores, carrying grocery bags, bathing, and dressing. [31]

Global Symptom Score (GSS) The numerical sum of five common carpal tunnel syndrome symptoms (pain, numbness, paraesthesia, weakness/clumsiness, and nocturnal wakening), which are each rated from 0 (no symptoms) to 10 (severe symptoms), to give a score of between 0 and 50. [70] [22]

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Symptom Severity Scale (SSS) Has 11 items concerning pain, nocturnal symptoms, numbness, tingling, and weakness. [31]

Tinel's test/sign Tingling in the median nerve distribution is induced by percussing the median nerve.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Corticosteroids (local injection) One systematic review updated (search date 2006) [13] and one systematic review added (search date 2006). [14] The first systematic review found that local corticosteroid injection increased the proportion of people with clinical improvement at 1 month or less, and improved symptoms at 6 weeks, compared with placebo. It also found that local corticosteroids improved symptom severity after 1 month, 8 weeks, and 12 weeks, compared with systemic corticosteroids. The second systematic review identified one additional RCT comparing corticosteroid injection versus placebo or no treatment, but the RCT did not perform between-group comparisons. Categorisation unchanged (Likely to be beneficial).

Corticosteroids (systemic) One systematic review added (search date 2002), [21] which identified no new RCTs to those previously reported in this *Clinical Evidence* review. Categorisation unchanged (Likely to be beneficial).

Diuretics One systematic review added (search date 2002), [21] which identified no new RCTs to those previously reported in this *Clinical Evidence* review. Categorisation unchanged (Unknown effectiveness).

Endoscopic versus open carpal tunnel release One systematic review (search date 2006) [39] updated and one subsequent RCT [40] added. The systematic review and subsequent RCT found that endoscopic and open carpal tunnel release may be equally effective at improving symptoms of CTS and improving hand function, and that endoscopic carpal tunnel release may shorten the time to return to work or activities of daily living compared with open carpal tunnel release. However, both types of surgery are associated with adverse effects. Categorisation unchanged (Trade-off between benefits and harms).

Internal neurolysis in conjunction with open carpal tunnel release One systematic review updated (search date 2006), [39] which identified no new RCTs to those previously reported in this *Clinical Evidence* review. Categorisation unchanged (Unlikely to be beneficial).

NSAIDs One systematic review added (search date 2002), [21] which identified no new RCTs to those previously reported in this *Clinical Evidence* review. Categorisation unchanged (Unknown effectiveness).

Pyridoxine One systematic review added (search date 2002), [21] which identified no new RCTs to those previously reported in this *Clinical Evidence* review. Categorisation unchanged (Unknown effectiveness).

Surgery versus local corticosteroid injection One systematic review (search date 2008) updated. [61] The review identified two RCTs with conflicting results. The first RCT found that local corticosteroid injection was more effective than surgery at improving nocturnal paraesthesia at 3 months, but the difference was not significant at 6 months. The second RCT found that surgery improved clinical outcome at 20 weeks compared with local corticosteroid injection; however, the review found no significant difference between the groups in grip strength at 20 weeks. Categorisation unchanged (Trade-off between benefits and harms).

Surgery versus wrist splint One systematic review updated (search date 2008), [61] which identified no new RCTs to those previously reported in this *Clinical Evidence* review. Categorisation unchanged (Trade-off between benefits and harms).

Therapeutic ultrasound One systematic review added (search date 2002), [21] which identified no new RCTs to those previously reported in this *Clinical Evidence* review. Categorisation unchanged (Unknown effectiveness).

Wrist splints One systematic review (search date 2002) [21] and one subsequent RCT [33] added. The systematic review identified no new RCTs to those previously reported in this *Clinical Evidence* review. The subsequent RCT compared neutral-angle splint, neutral-angle splint with nerve gliding exercises, wrist cock-up splint, and wrist cock-up splint with nerve gliding exercises; however, the RCT did not perform between-group comparisons and is of low quality, and therefore results are difficult to interpret. [33] Categorisation unchanged (Unknown effectiveness).

Nerve and tendon gliding exercises One systematic review (search date 2008) [29] and one subsequent RCT [30] added, which compared nerve and/or tendon gliding exercises plus wrist splints versus wrist splints alone. The systematic review and subsequent RCT found no significant differences between nerve and/or tendon gliding exercises plus wrist splints and wrist splints alone in most outcomes for symptom severity and hand function. Categorisation therefore changed from "Unknown effectiveness" to "Unlikely to be beneficial".

Surgery versus placebo Evidence reassessed; intervention recategorised from "Trade-off between benefits and harms" to "Unknown effectiveness".

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Competing interests: NA is a co-author of one systematic review referenced in this review. [13]

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TABLE 1 **Endoscopic versus open carpal tunnel release for the treatment of carpal tunnel syndrome**

Ref	Study population	Symptoms at 3 months or less	Symptoms at more than 3 months	Return to work/activities of daily life
[38]	Systematic review; search date 2001/2002; 12 RCTs; 1388 people	Pain at 12 weeks, 4 RCTs, pooled OR 3.092, 95% CI 0.693 to 13.803	NA	Time taken to return to work, 3 RCTs, pooled OR 1.516, 95% CI 0.276 to 8.341
		Grip strength at 12 weeks, 3 RCTs, pooled effect size: 0.68, 95% CI 0.06 to 1.30		
		Pinch strength at 12 weeks, pooled effect size: 0.38, 95% CI 0.09 to 0.66		
[39]	Systematic review; search date 2006, 19 RCTs, 1839 people	Symptom severity (as measured by the Levine scale) at 3 months or less, 3 RCTs, 451 people: mean difference –0.17, 95% CI –0.53 to +0.20. Statistical heterogeneity I^2 = 88%, P = 0.00022.	Symptom severity (as measured by the Levine scale) after more than 3 months, 2 RCTs, 275 people: mean difference 0, 95% CI –0.17 to +0.17	Time to return to work or activities of daily living, 3 RCTs, 294 people: mean difference –6.08 days, 95% CI –9.13 days to –3.03 days
		Function (as measured by the Levine scale) at 3 months or less, 3 RCTs, 451 people: mean difference –0.22, 95% CI –0.60 to –0.16. Statistical heterogeneity I^2 = 90%, P = 0.00003.	Functional (as measured by the Levine scale) after more than 3 months, 2 RCTs, 275 people WMD +0.08, 95% CI –0.06 to +0.22	
[48]	RCT; 30 people with bilateral CTS; 60 hands	Wound pain at 2 weeks (1–10 VAS): 3.3 with ECTR *v* 2.5 with OCTR with modified incision; P = 0.004	Wound or radial/ulnar pillar pain at 4, 6, and 12 months: data presented graphically; reported as NS	NA
		Wound pain at 4 weeks (1–10 VAS): 2.5 with ECTR *v* 1.5 with OCTR with modified incision; P = 0.008		
		Wound pain at 8 weeks: data not presented; reported as NS		
		Radial/ulnar pillar pain at 4 weeks: data presented graphically; reported as NS		
		Radial/ulnar pillar pain at 8 weeks: 16/30 (53%) with ECTR *v* 8/30 (27%) with OCTR with modified incision; P = 0.03		
[46]	RCT; 123 people; 150 hands	Pain score (anterior carpal tenderness score from 11 = painless to 55 = severe pain) at 3 months: 22 with endoscopic surgery *v* 24 with open surgery; P = 0.18	NA	Time to return to work (for 85/123 [69%] people in employment at baseline): 18 days with ECTR *v* 26 days with OCTR; mean difference: 8 days, 95% CI 2 days to 13 days
		Levine functional impairment score (8 = no impact to 40 = no activities possible) at 3 months: 109 with endoscopic surgery *v* 108 with open surgery; P = 0.98		
		Levine symptom score (11 = asymptomatic to 55 = severe symptoms) at 3 months: 120 with endoscopic surgery *v* 119 with open surgery; P = 0.70		

Ref	Study population	Symptoms at 3 months or less	Symptoms at more than 3 months	Return to work/activities of daily life
[50]	RCT; 128 people; 128 hands	Postoperative pain score determined by severity of pain in the scar and proximal palm and extent to which tenderness of scar limited activity (each rated on 4-point scale, which was transformed into a combined score of 0 = none to 100 = severe pain or tenderness causing severe limitation of activity). Mean change in postoperative pain score (from baseline) at 3 months: 23.5 with endoscopic surgery *v* 36.2 with open surgery; P = 0.001	Mean postoperative pain score at 12 months: 8.7 with endoscopic surgery *v* 13.9 with open surgery; P = 0.13	Median time to return to work for people not on sick leave before surgery (53/63 [84%] assigned to endoscopic surgery and 59/65 [91%] assigned to open surgery): 28 days with endoscopic surgery *v* 28 days with open surgery; P = 0.9 Median time taken to return to work for people on sick leave before surgery (10/63 [16%] assigned to endoscopic surgery *v* 6/65 [9%] assigned to open surgery): 51 days with endoscopic surgery *v* 37 days with open surgery; significance not assessed
		Mean severity of symptoms (assessed using CTS questionnaire; lower score indicates decreased severity of symptoms; mean change in score from baseline reported). Symptom severity scale score at 3 months: 1.5 with endoscopic surgery *v* 1.5 with open surgery; P = 0.44	Mean symptom severity scale score at 12 months: 1.4 with endoscopic surgery *v* 1.4 with open surgery; P = 0.96	Mean SF-12 score at 12 months: 50.1 with endoscopic surgery *v* 49.8 with open surgery; P = 0.78
		Mean functional status scale (assessed using CTS questionnaire) score at 3 months: 1.3 with endoscopic surgery *v* 1.3 with open surgery; P = 0.82	Mean functional status scale score at 12 months: 1.3 with endoscopic surgery *v* 1.2 with open surgery; P = 0.43	
		Grip score (measured by hand dynamometer): 31.5 with endoscopic surgery *v* 29.9 with open surgery; P = 0.69		
		Pinch score (measure by pinch gauge): 6.7 with endoscopic surgery *v* 6.0 with open surgery; P = 0.15		
[58]	RCT; 26 people; 36 hands	Improvement at 3 months: ECTR greater than OCTR with a modified incision; absolute numbers NR; reported as significant	NA	NA
[53] [54]	RCT; 45 people; 79% female; mean duration of symptoms 9 months	NA	NA	Mean: 24 days with ECTR *v* 42 days with OCTR; reported as significant
[47]	RCT; 40 hands; 20 matched pairs	Pain completely relieved at 3 months: 20/20 (100%) hands with ECTR *v* 15/20 (75%) hands with OCTR; significance assessment NR	Pain completely relieved after 8 months: 20/20 (100%) hands with ECTR *v* 19/20 (95%) hands with OCTR; significance assessment NR	Mean: 20 days with ECTR *v* 30 days with OCTR; reported as significant
		Persisting paraesthesiae at 3 months: 1/20 (5%) hands with ECTR *v* 1/20 (5%) hands with OCTR; significance assessment NR	Persisting paraesthesiae after 8 months: 1/20 (5%) hands with ECTR *v* 1/20 (5%) hands with OCTR; significance assessment NR; reported as NS by review [39]	
[41]	RCT; 145 people; 169 hands	Improvement in paraesthesiae and numbness after 12 weeks: 99% with ECTR *v* 98% with OCTR; difference +1%, 95% CI −3% to +5%	NA	Median: 14 days with ECTR *v* 28 days with OCTR; reported as significant
[43]	RCT; 71 people; 104 hands	Improvement in pain after 1, 2, and 4 weeks: ECTR greater than OCTR; absolute numbers NR; reported as significant	Improvement in pain after 6 months: absolute numbers NR; reported as NS	Mean: 14 days with ECTR *v* 39 days with OCTR; reported as significant
		Improvement in pain at 3 months: absolute numbers NR; reported as NS	Improvement in pain after 12 months: absolute numbers NR; reported as NS	
[51]	RCT; 29 people; 32 hands	NA	NA	Mean: 17 days with ECTR *v* 19 days with OCTR; reported as NS

Ref	Study population	Symptoms at 3 months or less	Symptoms at more than 3 months	Return to work/activities of daily life
[56]	RCT; 249 people; 251 hands; 54 with ECTR *v* 197 with OCTR	NR	NR	17 days with ECTR *v* 17 days with OCTR; reported as NS
[57]	RCT; 178 people	Mean symptom severity score at 3 months: 1.6 with ECTR *v* 1.5 with OCTR; reported as NS	NA	Proportion of people absent from work more than 4 weeks: 16% with ECTR *v* 13% with OCTR; difference: +3%, 95% CI −7% to +14%
[52]	RCT; 122 people; 147 hands	Data not reported separately	Data not reported separately	Median: 25.0 days with ECTR *v* 46.5 days with OCTR; reported as significant
[42]	RCT; 103 people; 60 with ECTR *v* 43 with OCTR	Persisting paraesthesiae at 3 months: 12% with ECTR *v* 7% with OCTR; significance assessment NR	Proportion of people with paraesthesiae after 6 months: 0% with ECTR *v* 0% with OCTR; significance assessment NR; reported as NS by review [39]	Proportion of people returned to work at 1 month: 45% with ECTR *v* 72% with OCTR; P = 0.13
		Persisting pain at 3 months: 38.5% with ECTR *v* 43.3% with OCTR; P = 0.71	Proportion of people with persisting pain after 6 months: 25% with ECTR *v* 28% with OCTR; significance assessment NR	Proportion of people returned to work at 3 months: 72% with ECTR *v* 90% with OCTR; reported as NS
[44]	RCT; 25 people; 50 hands	Jebson scores at 3 months: 75 with ECTR *v* 65 with OCTR; reported as NS	Jebson scores after 12 months: 59 with ECTR *v* 48 with OCTR; significance assessment NR; reported as NS by review [39]	NA
[45]	RCT; 123 people	Pain (McGill score) after 12 weeks: 8 with ECTR *v* 12 with OCTR; reported as NS	Patient satisfaction scores after a mean 3.2 years: 85% with ECTR *v* 93% with OCTR; significance assessment NR; reported as NS by review [39]	Absolute numbers NR; reported as NS
		Symptom severity (Levine score) after 12 weeks: 1.8 with ECTR *v* 2.0 with OCTR; reported as NS		
		Functional status (SF-36 score) after 12 weeks: 47 with ECTR *v* 42 with OCTR; reported as NS		
[55]	RCT; 147 people; 192 hands	Patient satisfaction score at 3 months: 4.4 with ECTR *v* 4.0 with OCTR; reported as NS	Patient satisfaction score after 12 months: 4.6 with ECTR *v* 4.5 with OCTR; reported as NS	Median: 18 days with ECTR *v* 38 days with OCTR; reported as significant
		Symptom severity (Levine scale) at 3 months: 1.8 with ECTR *v* 2.5 with OCTR; reported as significant	Symptom severity (Levine scale) after 12 months: 1.8 with ECTR *v* 1.8 with OCTR; reported as NS	
		Functional status (Levine scale) at 3 months: 1.7 with ECTR *v* 2.4 with OCTR; reported as significant	Functional status (Levine scale) after 12 months: 1.7 with ECTR *v* 1.7 with OCTR; reported as NS	
Data for this RCT extracted from systematic review [39]	RCT; 80 people; 80 hands	Symptom severity score (variant of Levine) at 3 months: 11.0 with ECTR *v* 10.6 with OCTR; reported as NS		Mean: 34.5 days with ECTR *v* 36 days with OCTR; reported as NS
		Mean functional status score (variant of Levine) at 3 months: 10.2 with ECTR *v* 9.8 with OCTR; reported as NS		

Ref	Study population	Symptoms at 3 months or less	Symptoms at more than 3 months	Return to work/activities of daily life
Data for this RCT extracted from systematic review [39]	RCT; 227 people. Three-arm trial comparing ECTR (110 people; 125 hands) *v* OCTR (54 people, 60 hands) *v* OCTR with modified incision (63 people; 65 hands)	NA	Mean overall severity score using a scale of 1–6 after more than 1 year: 2.1 with ECTR *v* 2.2 with OCTR; reported as NS	NA
			Mean overall severity score using a scale of 1–6 after more than 1 year: 2.1 with ECTR *v* 2.2 with OCTR with modified incision; reported as NS	
[40]	RCT; 62 people, 72 hands	Improvement in 2-point discrimination from pre-operation to post-operation (time of postoperative assessment not clear): 0.6 mm with ECTR *v* 1.9 mm with OCTR; P greater than 0.05	Proportion of people rating their satisfaction as excellent or good at about 2 years: 93.2% with ECTR *v* 91.5% with OCTR (absolute results NR); P greater than 0.05	Time to return to work: 12 days with ECTR *v* 28 days with OCTR; P less than 0.01

ECTR, endoscopic carpal tunnel release surgery; NA, not assessed; NR, not reported; NS, reported as not significant; OCTR, open carpal tunnel release surgery; Ref, reference; SF, short form; VAS, visual analogue scale.

TABLE **GRADE evaluation of interventions for carpal tunnel syndrome**

Important outcomes		Symptoms of carpal tunnel syndrome, hand function, time to return to work, adverse effects							
Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of drug treatments for carpal tunnel syndrome?									
4 (257) [13] [15] [21]	Symptom severity	Local corticosteroid injection *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for use of an unvalidated outcome scale
2 (97) [17] [18]	Symptom severity	Local corticosteroid injection *v* systemic corticosteroids	4	–2	0	0	0	Low	Quality points deducted for sparse data and use of an unvalidated outcome scale
2 (151) [61]	Symptom severity	Local corticosteroid injection *v* carpal tunnel release surgery	4	–1	–1	0	0	Low	Quality point deducted for sparse data. Consistency point deducted for conflicting results
1 (50) [61]	Hand function	Local corticosteroid injection *v* carpal tunnel release surgery	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
3 (90) [21]	Symptom severity	Systemic corticosteroids *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (48) [22]	Symptom severity	Systemic corticosteroids *v* NSAIDs	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (46) [22] [21]	Symptom severity	Systemic corticosteroids *v* diuretics	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (40) [23]	Symptom severity	Systemic corticosteroids *v* splints	4	–2	0	0	0	Low	Quality points deducted for sparse data and statistical flaws
1 (40) [23]	Hand function	Systemic corticosteroids *v* splints	4	–2	0	0	0	Low	Quality points deducted for sparse data and statistical flaws
2 (91) [22] [26] [21]	Symptom severity	Diuretics *v* placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and use of an unvalidated outcome scale
1 (42) [22] [21]	Symptom severity	Diuretics *v* NSAIDs	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (45) [22]	Symptom severity	NSAIDs *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (35) [28]	Symptom severity	Pyridoxine *v* placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and use of an unvalidated outcome scale
What are the effects of non-drug treatments for carpal tunnel syndrome?									
4 (176) [31] [32] [33] [30]	Symptom severity	Nerve/tendon gliding exercise plus splint *v* splint alone	4	–2	–1	0	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Consistency point deducted for differences in intervention type and duration
1 (176) [31] [32] [33] [30]	Hand function	Nerve/tendon gliding exercise plus splint *v* splint alone	4	–2	–1	0	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Consistency point deducted for differences in intervention type and duration
1 (45) [34]	Symptom severity	Therapeutic ultrasound *v* placebo	4	–3	0	0	0	Very low	Quality points deducted for sparse data, use of an unvalidated outcome scale, and statistical flaws

Important outcomes	Symptoms of carpal tunnel syndrome, hand function, time to return to work, adverse effects								
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
1 (83) [35]	Symptom severity	Wrist splint *v* no treatment	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
2 (198) [61] [62]	Symptom severity	Wrist splints *v* carpal tunnel surgery	4	–2	0	0	0	Low	Quality points deducted for sparse data and methodological flaws
1 (24) [37]	Symptom severity	Full-time use of splint *v* nocturnal use alone	4	–2	0	0	0	Low	Quality points deducted for sparse data and poor compliance with treatment
1 (61) [33]	Symptom severity	Neutral splint v cock-up splint	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and statistical flaws. Directness point deducted for use of co-interventions
What are the effects of surgical treatments for carpal tunnel syndrome?									
At least 13 RCTs (at least 1457 people) [38] [39] [41] [42] [43] [45] [46] [47] [48] [40] [55] [57]	Symptom severity	Endoscopic *v* open surgery	4	0	0	–1	0	Moderate	Directness point deducted for heterogeneity among studies
At least 6 RCTs (at least 608 people) [38] [39] [44] [45] [46] [40] [55]	Hand function	Endoscopic *v* open surgery	4	0	0	–1	0	Moderate	Directness point deducted for heterogeneity among studies
At least 15 RCTs (at least 1645 people) [38] [39] [41] [42] [43] [45] [46] [47] [40] [52] [53] [54] [55] [56] [57]	Time to return to work	Endoscopic *v* open surgery	4	0	0	–1	0	Moderate	Directness point deducted for heterogeneity among studies
3 (148) [64] [65] [66]	Symptom severity	Internal neurolysis plus open carpal tunnel release *v* open carpal tunnel release alone	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for uncertainty about interventions
What are the effects of postoperative treatments for carpal tunnel syndrome?									
1 (47) [68]	Symptom improvement	Wrist splints after surgery *v* no movement restriction	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and poor follow-up. Directness point deducted for uncertain outcome measure
1 (74) [67]	Hand function	Wrist splints after surgery *v* no movement restriction	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (50) [69]	Return to work	Wrist splints after surgery *v* no movement restriction	4	–1	0	0	0	Moderate	Quality point deducted for sparse data

Type of evidence: 4 = RCT; 2 = Observational; 1 = Non-analytical/expert opinion.
Consistency: similarity of results across studies.
Directness: generalisability of population or outcomes.
Effect size: based on relative risk or odds ratio.