Figure 1. Location of the carpal tunnel

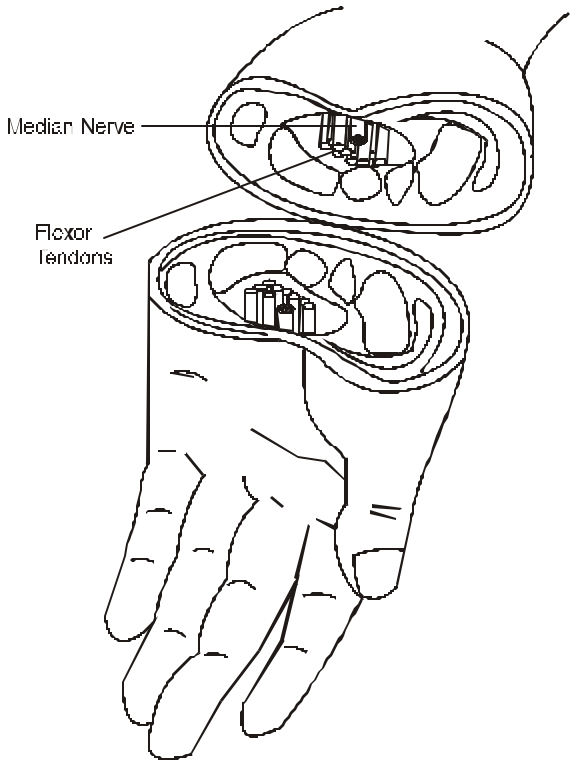
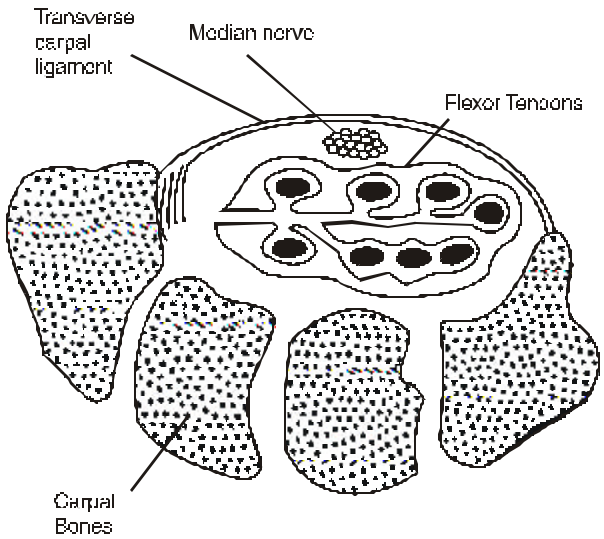


Figure 2. Structures associated with carpal tunnel syndrome



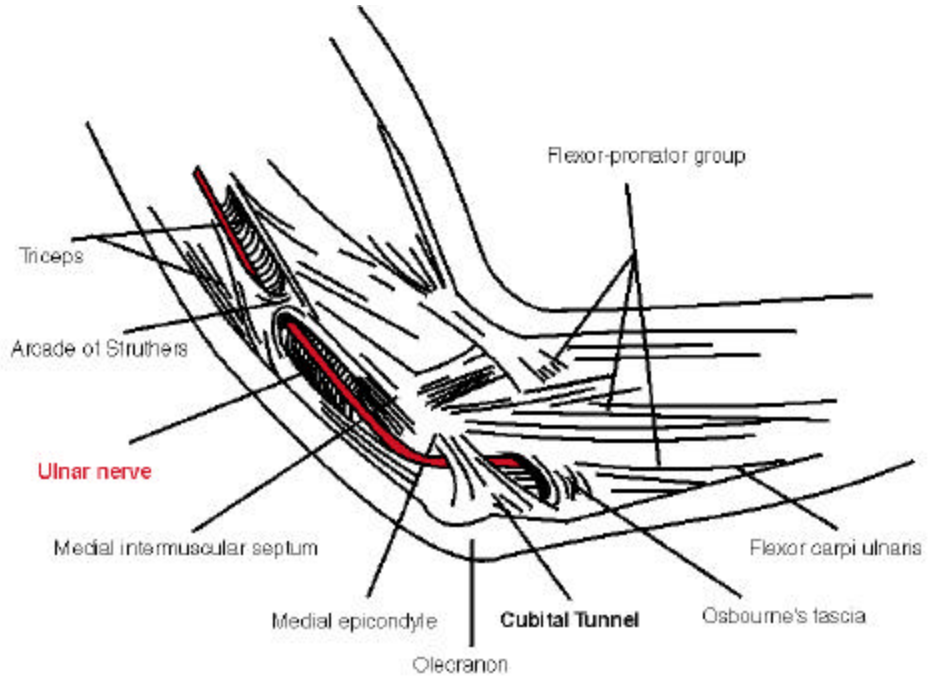
Etiology

Carpal tunnel syndrome is often idiopathic. The most common attributed cause of CTS is tenosynovitis or hypertrophy of the tendon sheaths of the finger flexor tendons due to overuse, often from the repetitive hand motions associated with

Anatomy

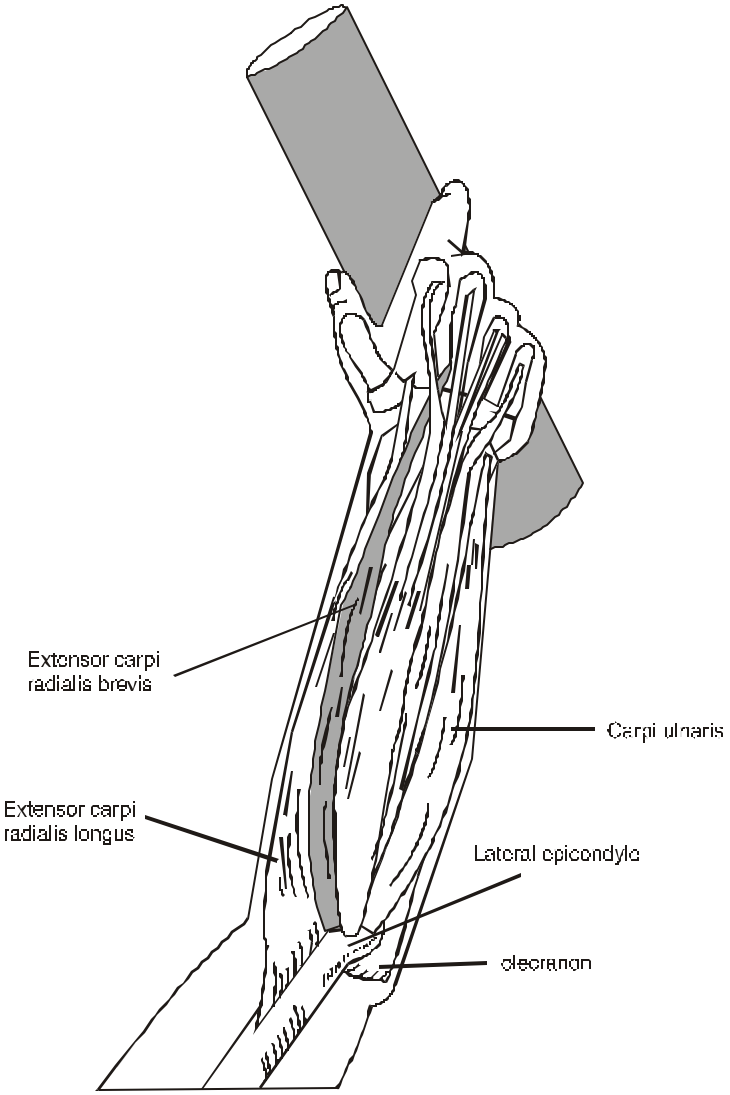
The ulnar nerve carries nerve fibers from the eighth cervical and first thoracic nerves. It passes down the upper arm medial to the brachial artery, then passes through the intermuscular septum and travels towards the elbow near the medial head of the triceps. At the elbow, the ulnar nerve passes behind the medial epicondyle of the humerus in a groove between it and the heads of the flexor carpi ulnaris, the cubital tunnel. The ulnar nerve then enters the forearm between the two heads of the flexor carpi ulnaris muscle and enters the hand.[57-59] It is not until the ulnar nerve passes between the two heads of the flexor carpi ulnaris muscle that it begins supplying motor and sensory innervation. It supplies motor innervation to the muscles of the forearm and hand, and sensory innervation to the medial half of the hand, the palm, and the fourth and fifth digits.[57]

Figure 3. The cubital tunnel and associated structures



The groove that the ulnar nerve passes through at the elbow is referred to as the cubital tunnel. This tunnel is bounded by the medial epicondyle of the humerus anteriorly (See Figure 3), the ulnohumeral ligament laterally, and posteromedially, a fibrous arcade of fascial strands that extends from the olecranon to the medial epicondyle, bridging the two heads of the flexor carpi ulnaris muscle.[57,58] Under normal conditions, the capacity of the ulnar tunnel is greatest during elbow extension. Flexion of the elbow decreases the volume of the cubital tunnel by tightening the arcuate ligament, bulging of the medial elbow ligament, and contraction of the flexor carpi ulnaris muscle.[58]

Figure 4. Structures associated with lateral epicondylitis

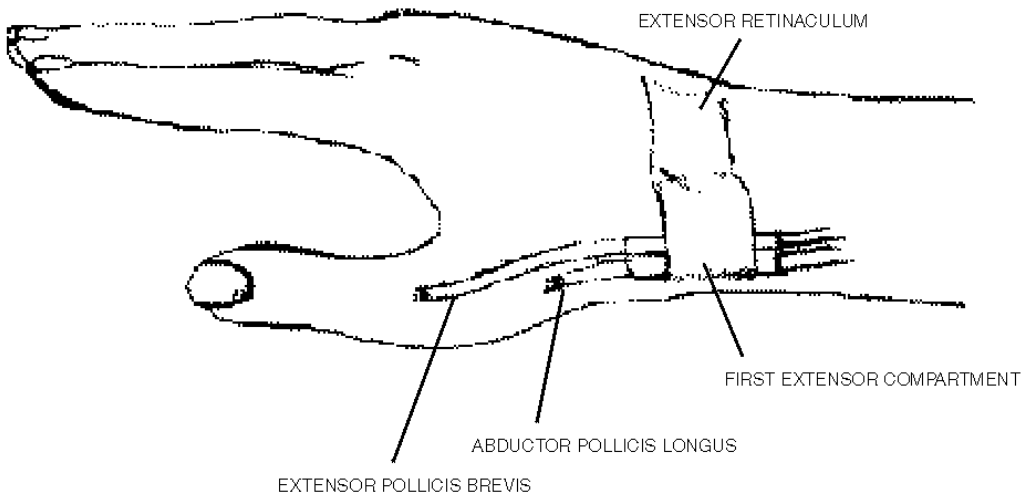


The exact pathology that underlies epicondylitis is not known.[70] The problem appears to be confined to the tendinous and fascial attachments to the bone (See Figure 4). The tendons become dull, gray, friable, and edematous. The normal tendon fibers become disrupted by invading fibroblasts and granulation tissue.[78] Adhesions may form between the tendon and surrounding tissues. The extensor carpi radialis brevis tendon appears to be most often affected because it is intimately attached to the joint capsule, and because of this proximity adhesions readily form between it and the joint.

Anatomy

De Quervain's disease is a stenosis (thickening) of the fibrous sheath of the first extensor compartment of the extensor retinaculum.[86] This compartment surrounds two tendons, the extensor pollicis brevis and the abductor pollicis longus (See Figure 5). In the past, de Quervain's disease has been described as a type of stenosing tenosynovitis of the hand and wrist. Because recent studies have shown that there is no inflammatory process associated with de Quervain's disease, some experts believe that the term tenosynovitis is not accurate for describing this condition.[53,86]

Figure 5. Structures associated with De Quervain's disease



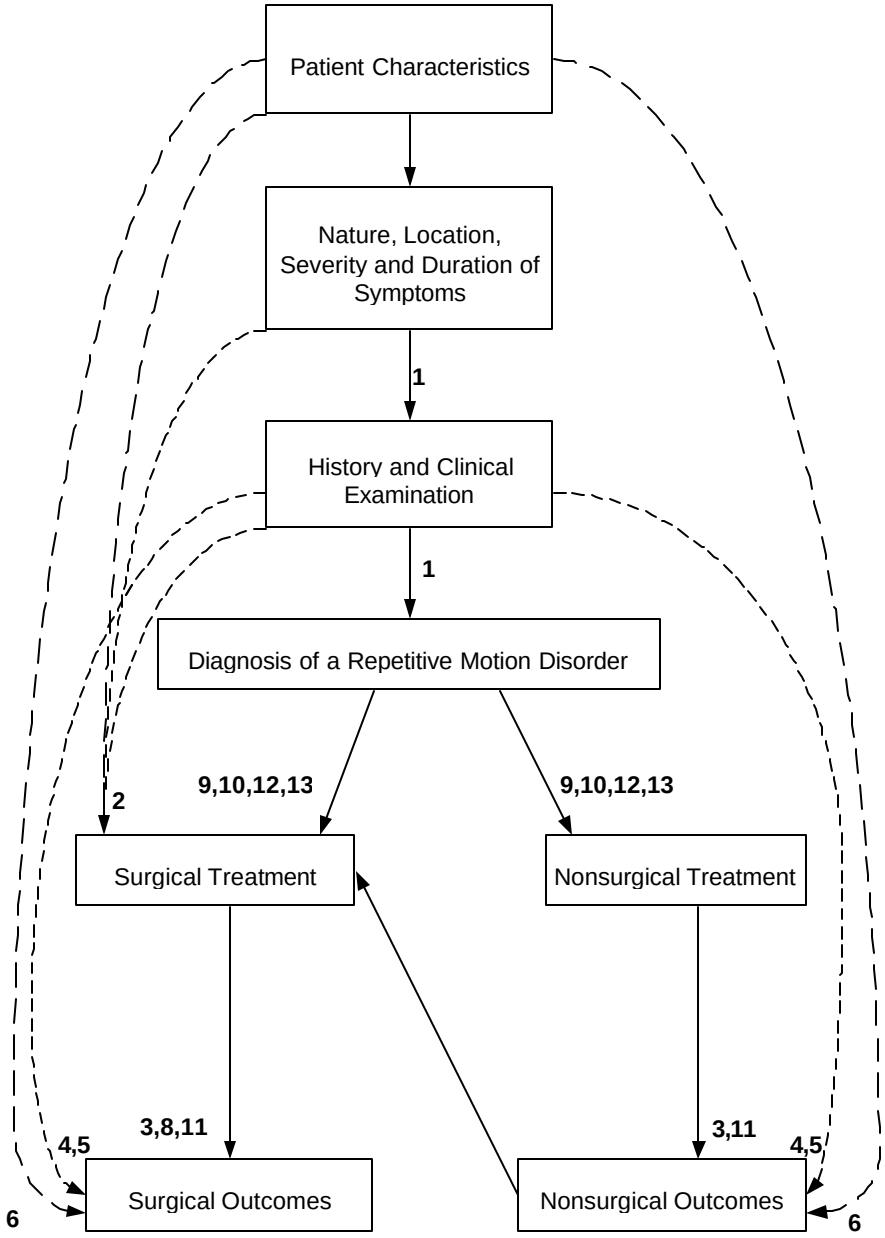
Etiology

Possible etiologic factors include acute trauma, recurrent trauma, or an underlying collagen disease.[87]

Epidemiology

De Quervain's disease appears most frequently in the 30 to 50 year age group and has been reported to be 10 times more common among women than men.[85] Work occupations commonly associated with this condition include musicians, weavers, typists, nurses, knitters, golfers, switchboard operators, and manual workers.[53,85] However, there is disagreement among experts as to whether these types of work cause de Quervain's disease or merely exacerbate the symptoms.[53,86] Anatomic variations of the first extensor compartment have also been reported to be associated with de Quervain's disease.[86]

Figure 6. Causal Pathway



Literature Searches

Our searches for information were designed to produce a comprehensive dataset. Therefore, we searched a number of electronic databases and other sources. These are described below.

Figure 7. Mean Ages of Patient and Control Groups in CTS Diagnostic Studies

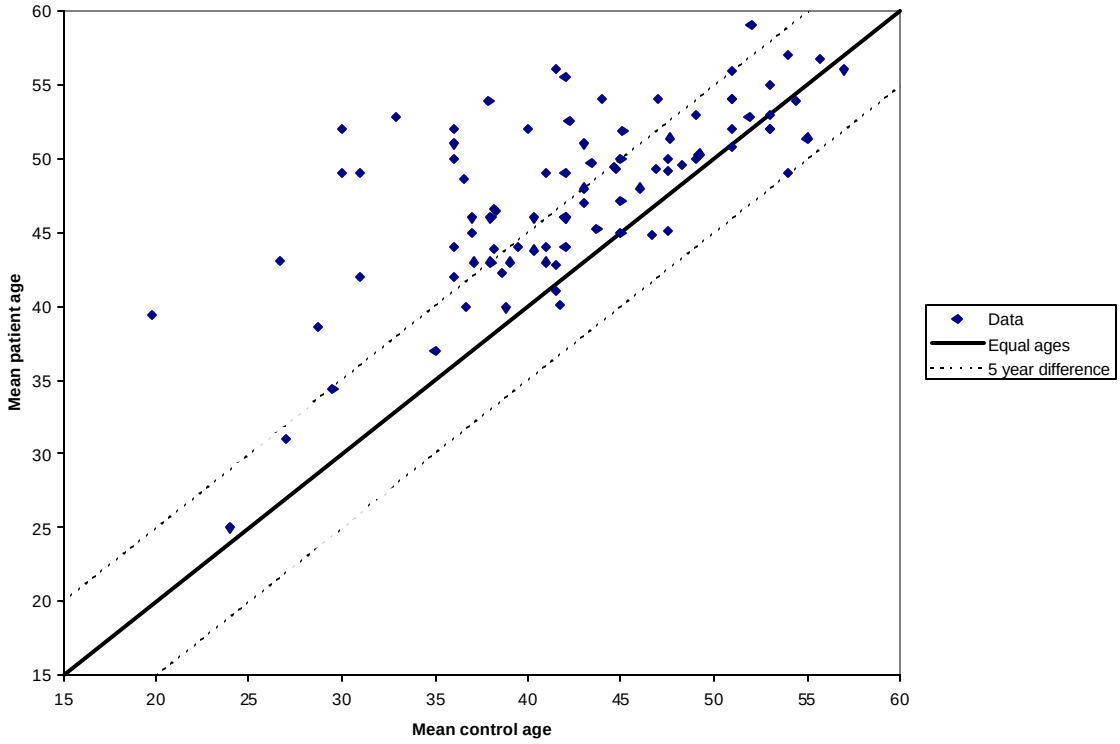


Figure 8. Sex Ratios of Patient and Control Groups in CTS Diagnostic Studies

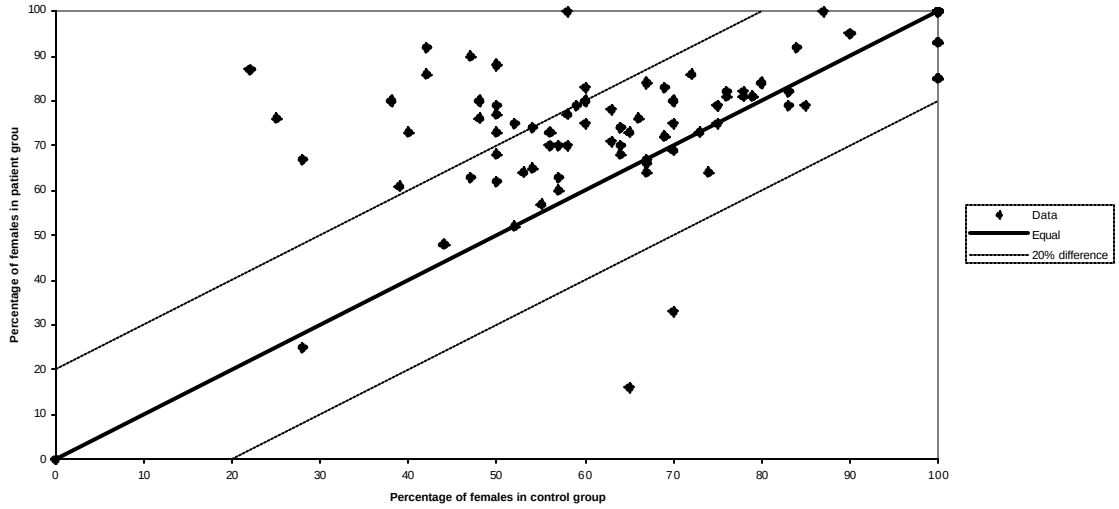
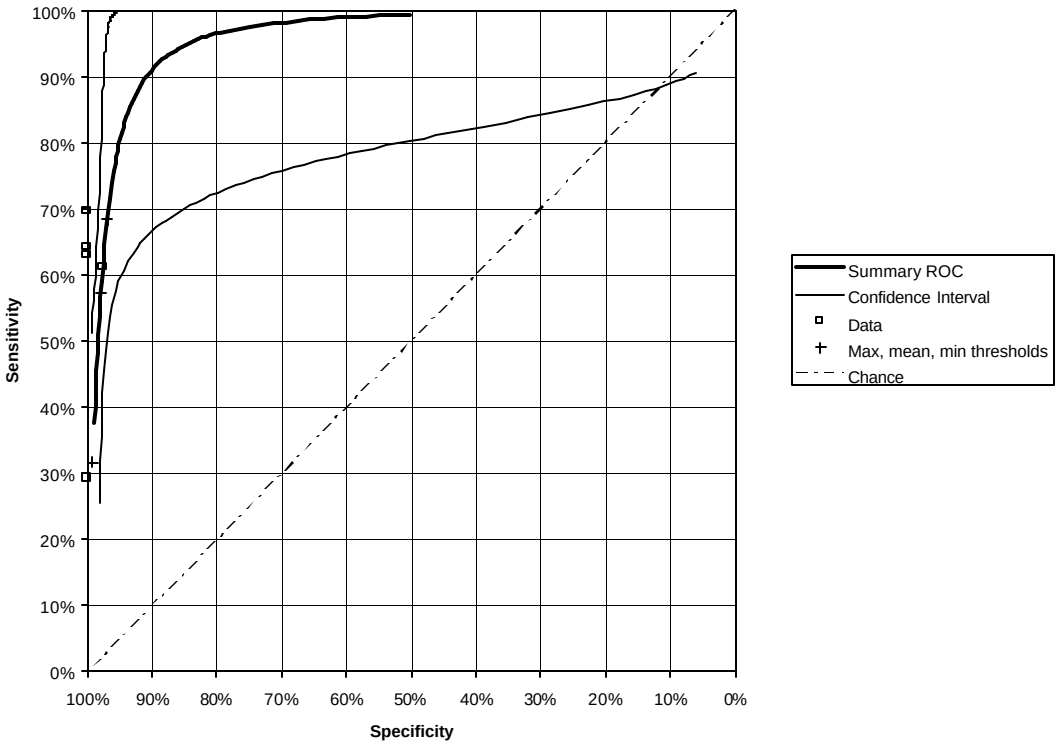


Figure 9. Meta-analysis of Distal Motor Latency Results in Trials With Non-specific Diagnosis of Carpal Tunnel Syndrome Groups

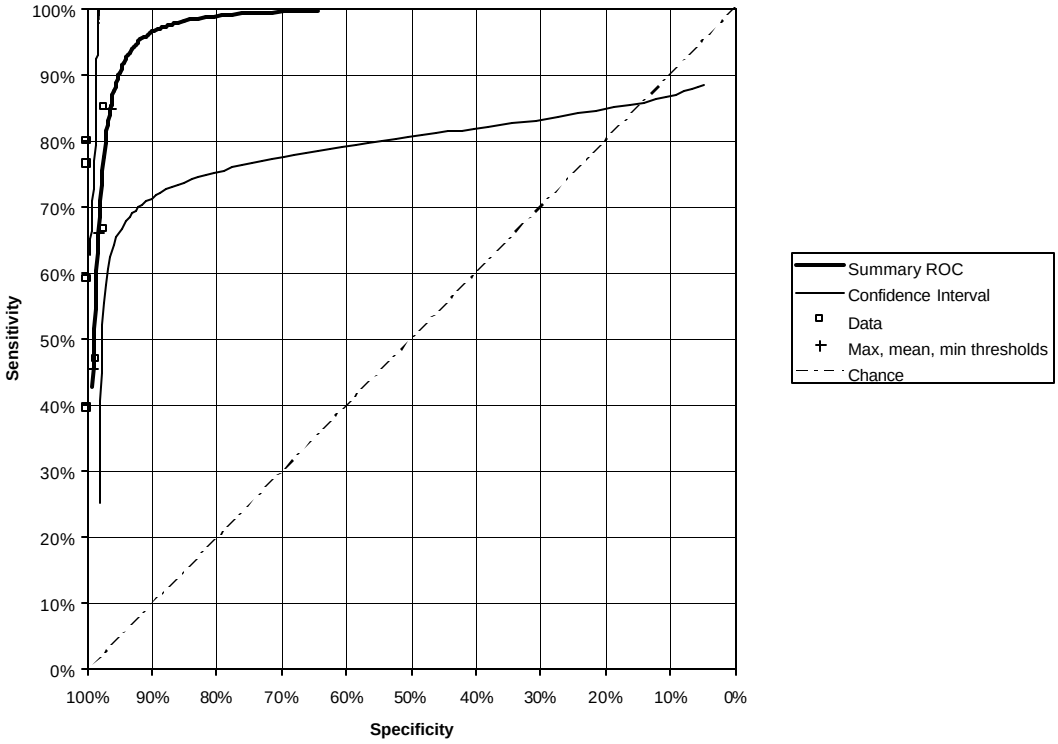


Distal Motor Latency: Patients with Symptoms of CTS v. Normal Controls

Seventeen studies met the initial criteria for inclusion in a meta-analysis of DML for distinguishing patients with symptoms of CTS from healthy volunteer controls. As with the meta-analysis on patients with unspecified diagnosis of CTS, there were several articles that did not include sufficient data to permit inclusion in the meta-analysis (Table 24). Four articles were excluded because they did not report the number of CTS patients with normal and abnormal DML, and two articles were excluded because they did not report the corresponding data for control subjects. Two articles were excluded due to selection bias: DML was one of their patient selection criteria. Another article was excluded because of discrepancies in the reported results; ECRI could not verify or recalculate the 2 x 2 table.

Eight articles remained after those exclusions (see Table 25). Significant heterogeneity in their results was found by the Q statistic ($Q = 16.7$, $p = 0.019$), with one obvious outlier (Atroshi et al.[136], standardized residual = –3.68). Excluding that study left the remaining results homogeneous ($Q = 3.15$, $p = 0.79$). The meta-analysis was completed both with and without the outlier included, and there was no substantial effect on the results. With the outlier excluded (Figure 10), the sensitivity/specificity at mean threshold was 66.0%/98.3%. Including the outlier changed the results by less than a percentage point: the sensitivity/specificity at mean threshold was 65.0%/97.7%.

Figure 10. Meta-analysis of Distal Motor Latency Results in Trials With Patients Presenting with CTS Symptoms



Note:
One outlier[136] was excluded (see text).

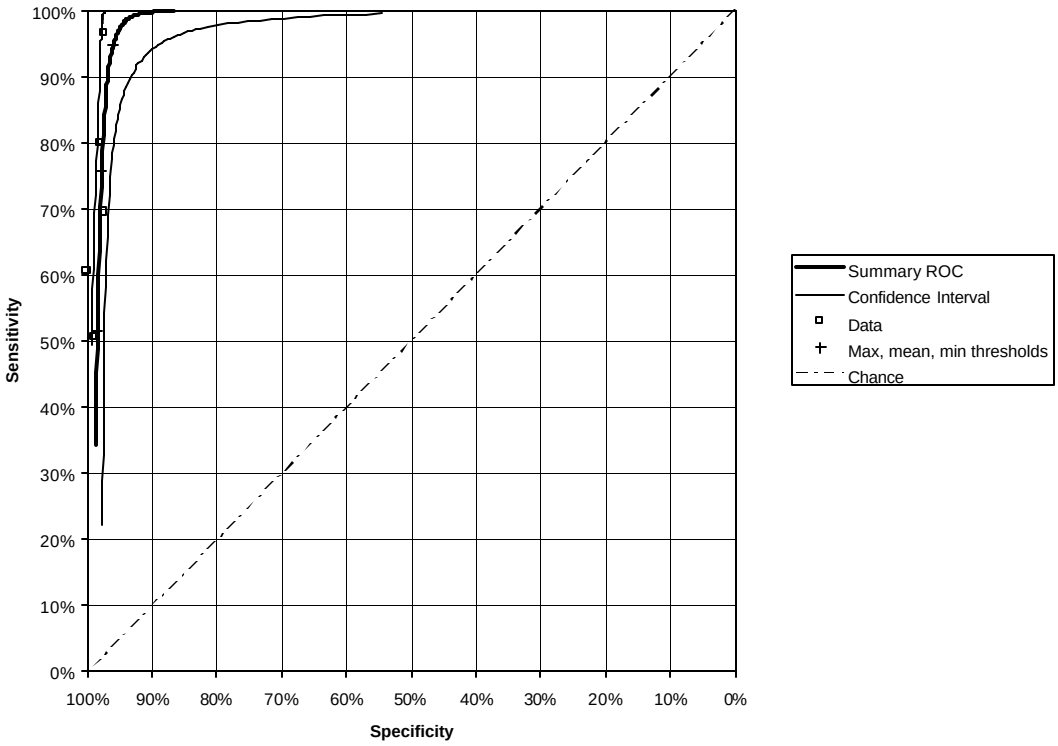
Palmar Sensory Latency: Patients with Symptoms of CTS v. Normal Controls

The cross-tabulation found 11 articles that included palmar sensory latency studies and reported some data in the form of a 2 x 2 table. The articles compared patients who presented with suspected CTS or symptoms of CTS to healthy normal controls. As with the other meta-analyses, several studies could not be included in the meta-analysis (Table 26). Five articles did not report sufficient data to allow us to calculate sensitivity and specificity for this particular test. One used palmar sensory latency as a patient selection criterion and was excluded due to selection bias.

After these exclusions, five studies remained in the meta-analysis. There was no statistically significant heterogeneity in their results ($Q = 4.87$, $p = 0.30$). The studies and their results are listed in Table 27 and the summary ROC plot is shown in Figure 11.

Like DML, palmar sensory latency has very high specificity. The normal volunteers studied in these trials rarely had abnormal results. This finding, however, does not reveal the test performance on persons with suspected CTS. To address that issue, a computation of sensitivity is required. The sensitivity/specificity at mean threshold was 75.8%/97.7%, and it is clear that the test has some ability to identify persons with

Figure 11. Meta-analysis of Palmar Sensory Latency Results



Phalen's Maneuver: Combined CTS Groups v. Normal Controls

There were no clinical signs or symptoms for which at least 10 articles reported sensitivity and specificity in a specific patient population. Therefore, we loosened the inclusion criteria by first combining the four patient selection categories, and then requiring a total of 20 or more sensitivity/specificity articles. Because none of the signs and symptoms data met that loosened criterion, we again lowered the threshold to a total of 15 studies or more. Two tests met that criterion: Phalen's maneuver and Tinel's sign. We proceeded to attempt meta-analysis of these data, recognizing that combining patient selection groups could cause heterogeneity of study results that could prevent meta-analysis.

The evidence base on Phalen's maneuver comprised 15 studies. Two of these reported two CTS groups, for a total of 17 entries in the cross-tabulation. For analyzing the two studies with two CTS groups,[101,154] we combined results of all CTS patients. Three articles were excluded because they did not report sufficient data to allow specificity to be calculated. Phalen's maneuver data from the article by Glass and King[28] was excluded because results were reported for only 22 of the 159 hands with CTS, and the authors did not report the reason for this. Finally, we determined while abstracting data that two publications by Gerr[31,197] reported the same controls and likely the same patients. Only the later publication[31] was included in the analysis. Excluded articles are listed in Table 28.

Figure 12. Diagnostic Trial Results for Phalen's Maneuver

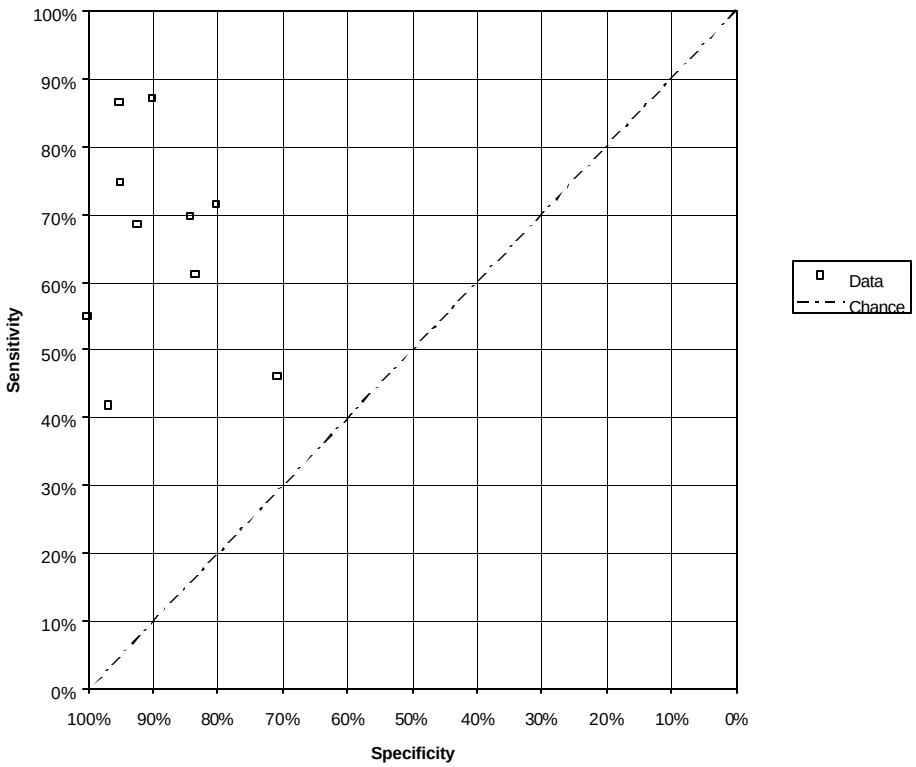
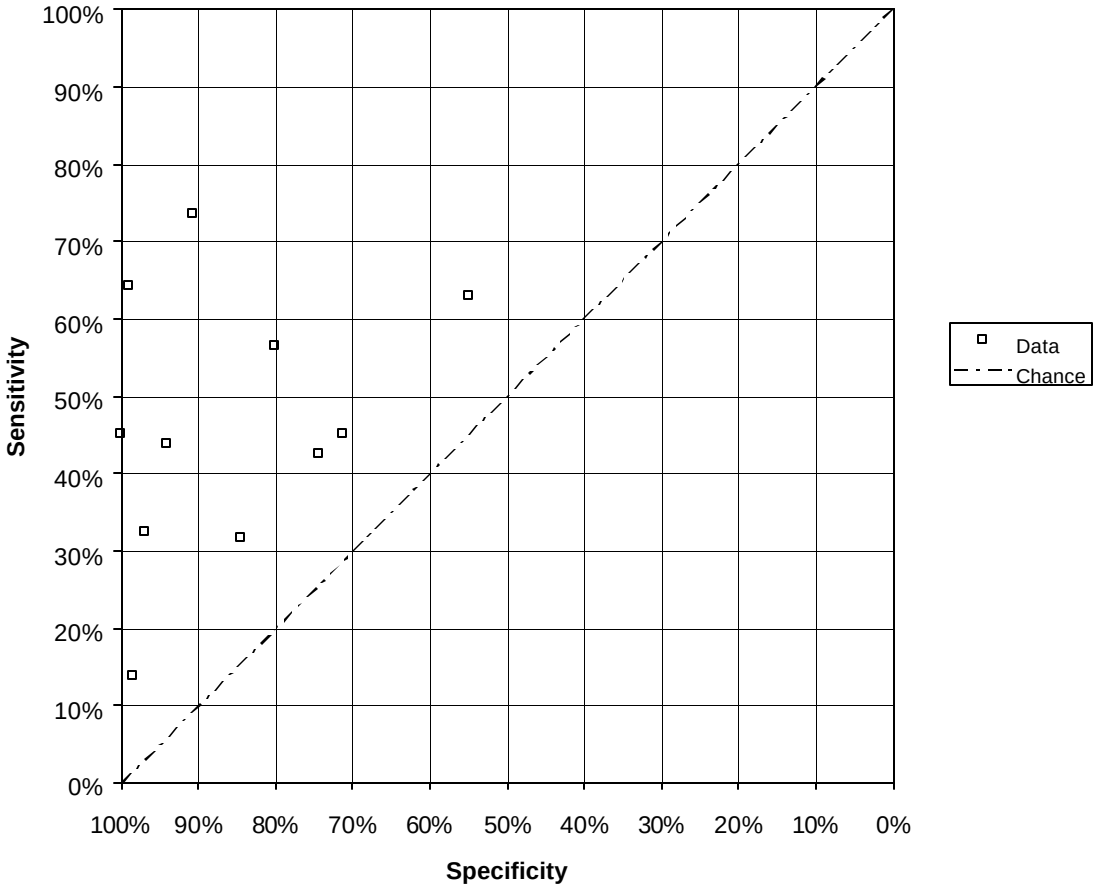


Table 30. Heterogeneity of Diagnostic Trial Results for Phalen's Maneuver

Group	Q (p-value) for larger group
All articles (N = 10)	71.4 (p <0.000001)
Patients selected with complex objective standard (N = 6) v. other selection	59.4 (p <0.000001)
Reverse Phalen's maneuver (N = 1) v. conventional	70.8 (p <0.000001)
Not funded by for-profit device or drug manufacturer (N = 4) v. not reported	58.5 (p <0.000001)
Reported both inclusion and exclusion criteria (N = 4) v. reported only inclusion criteria	20.5 (p = 0.001)
Prospective patient selection (N = 5) v. not reported	58.7 (p <0.000001)
Comorbidity reported (N = 1) v. not reported	69.9 (p <0.000001)
Sex ratios of patients, controls within 20% of each other (N = 5) v. possible sex bias	58.5 (p <0.000001)
Mean ages of patients, controls within 5 years (N = 3) v. possible age bias	15.4 (p = 0.017)
Duration of condition reported (N = 2) v. not reported	48.4 (p <0.000001)
Independent reference standard (N = 4) v. no independent reference standard reported	48.2 (p <0.000001)
Patients given both study test and reference test (N = 3) v. did not do so	49.3 (p <0.000001)
Studies done in USA (N = 6) v. other countries	58.1 (p <0.000001)
Potential selection bias for easy cases (N = 4) v. no bias or not reported	49.3 (p <0.000001)

Q—Q-statistic, with probability that variability in study results [D, logit (sensitivity) + logit (specificity)] is the result of random variability within a homogeneous sample of studies.

Figure 13. Diagnostic Trial Results for Tinel's Sign



Author, Year	Clinical findings			Nerve conduction studies						Comments
	SYM	CLN	OTH CLN	DML	DSL	PAL	SEN DIF	MOT DIF	OTH NCS	
Jetzer, 1991 [168]	☑	?	?	?	?	?	?	?	?	Or positive NCS (tests not reported)
DeKrom, 1990 [222]	☑	?	?	☑	?	?	☑	?	?	
Welch, 1973 [223]	?	?	?	?	?	?	?	?	?	NR
Totals	12	2	1	5	5	4	9	1	6	

Key
SYM—Were positive symptoms included in the author's method of diagnosis?
CLN—Was a positive clinical exam included in the author's method of diagnosis?
OTH CLN—Were other clinical findings included in the author's method of diagnosis?
DML—Was distal motor latency included in the author's method of diagnosis?
DSL—Was distal sensory latency included in the author's method of diagnosis?
PAL—Was palmar sensory latency included in the author's method of diagnosis?
SEN DIF—Was the difference between median and ulnar sensory studies included in the author's method of diagnosis?
MOT DIF—Was the difference between median and ulnar motor studies included in the author's method of diagnosis?
OTH NCS—Were other nerve conduction studies included in the author's method of diagnosis?
NR—Method of diagnosis was not reported

Figure 14. Association of Symptoms with Positive NCS Findings in Screening Studies

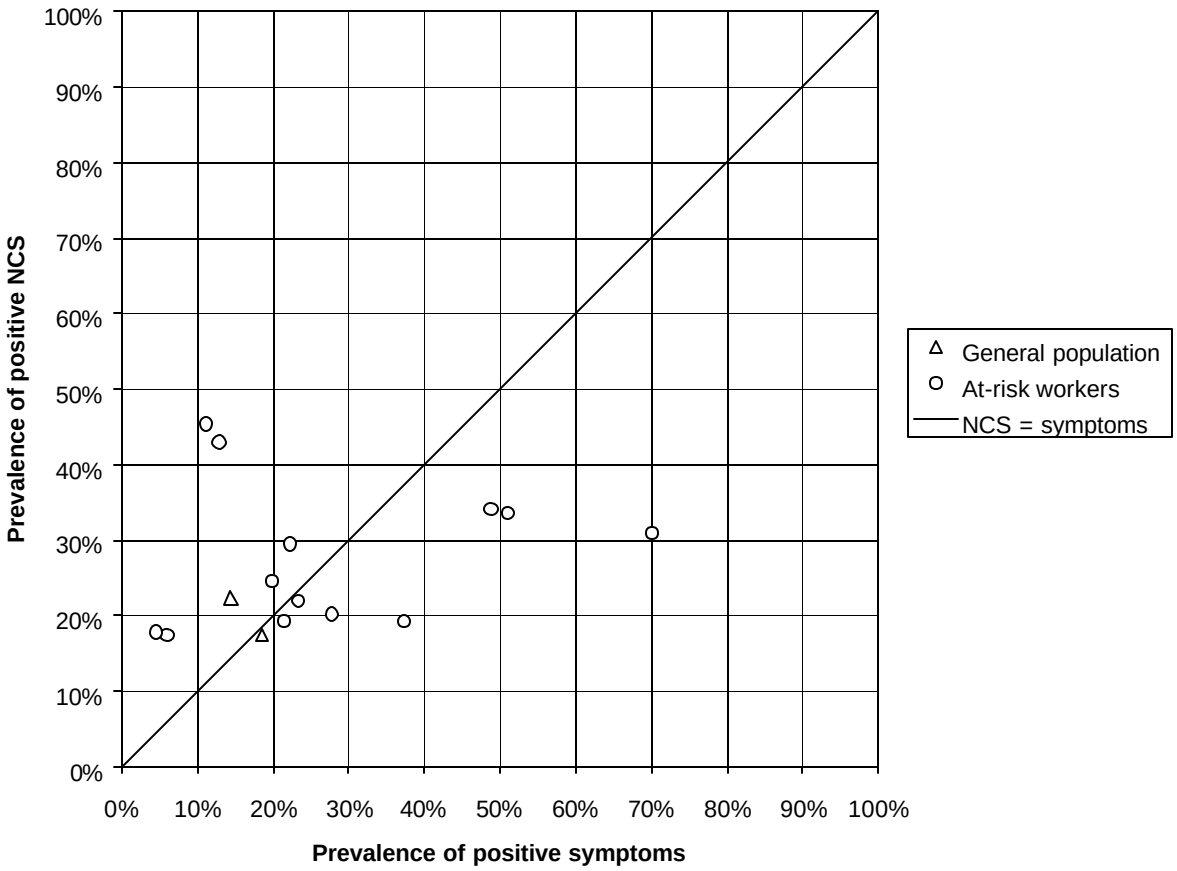
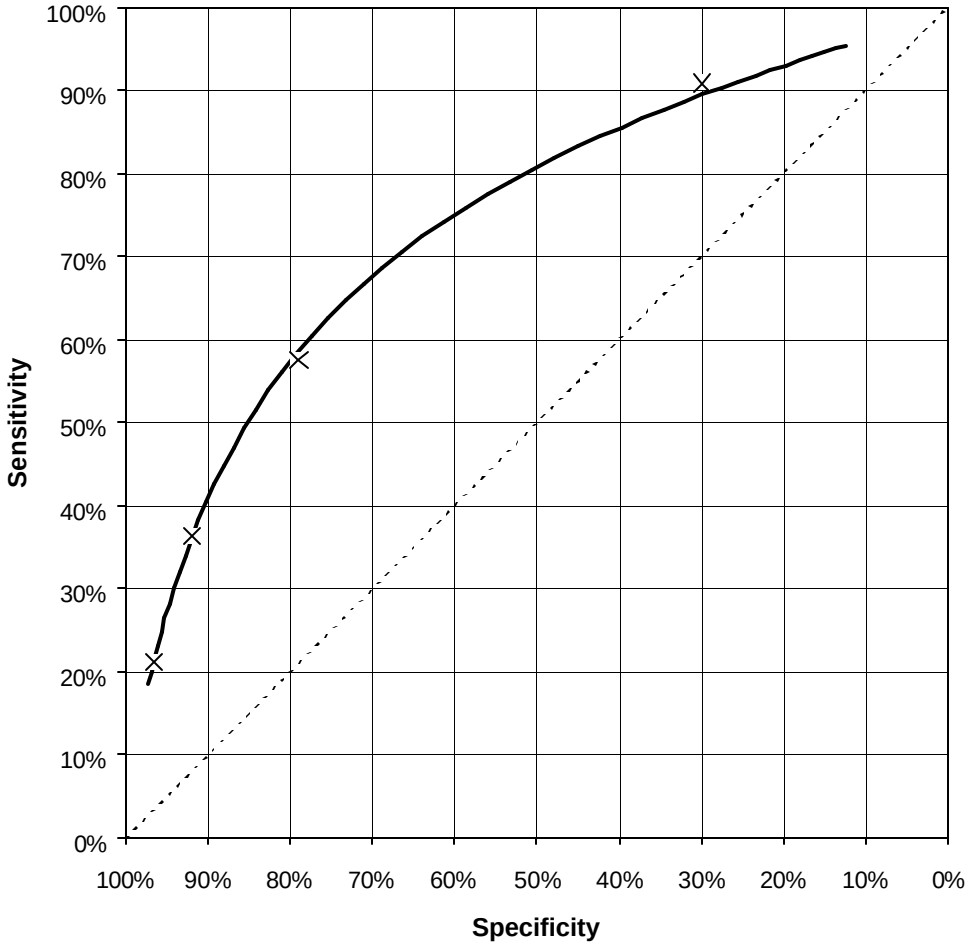


Figure 15. Prediction of Future CTS by Maximum Latency Difference



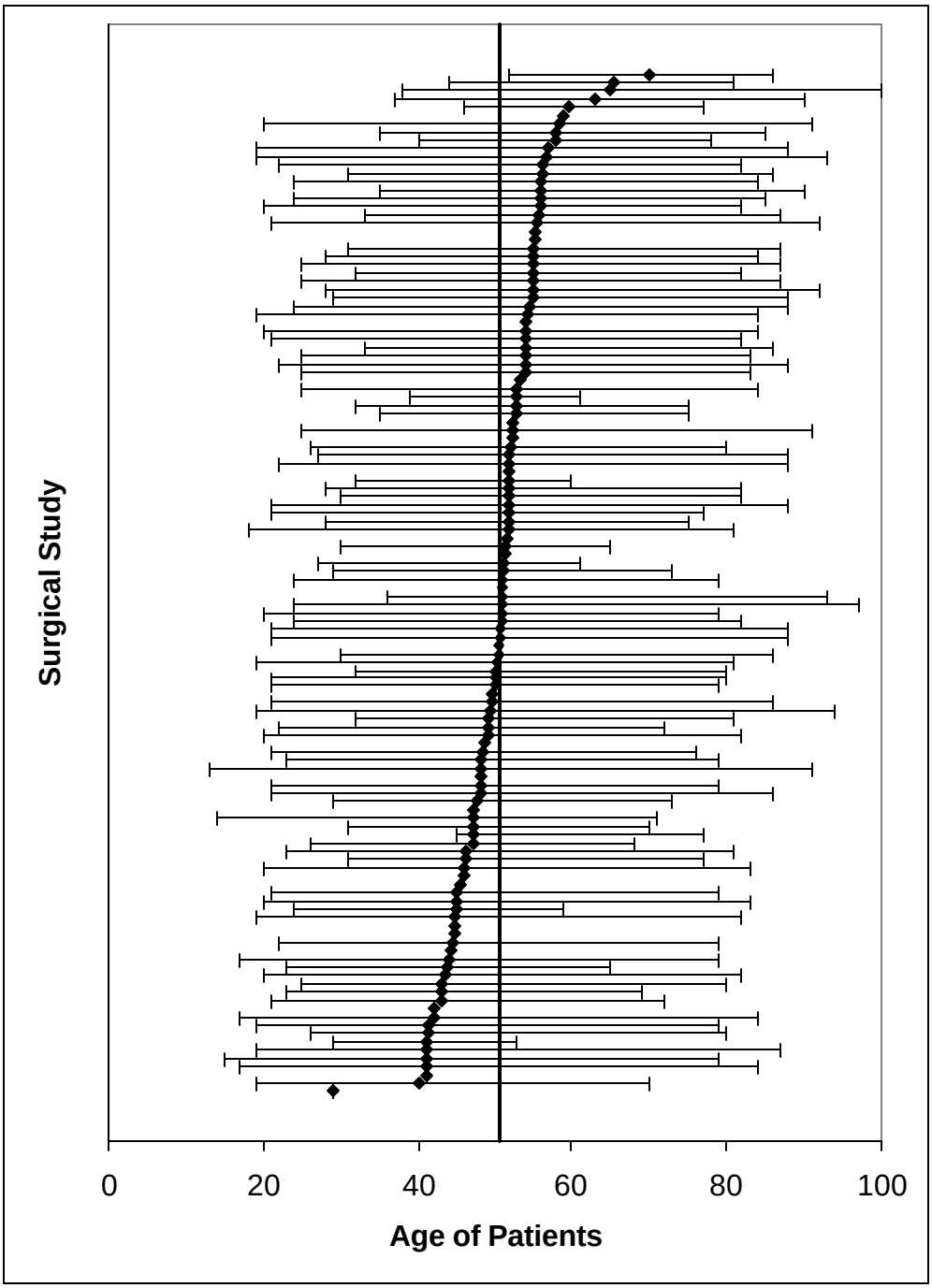
Data from Nathan et al.[202]

Conclusions

The evidence base on most individual diagnostic tests for carpal tunnel syndrome is small, even though the total number of articles on CTS diagnosis is large (Table 19). This is because there are so many different tests that have been reported. Nerve conduction tests are most frequently reported in the literature, but there is great diversity in their methods, and one cannot conclude that one of these tests is effective based on clinical trial results for another test.

The most frequently reported nerve conduction tests were distal motor latency and palmar sensory latency. There were sufficient clinical trial articles available for us to meta-analyze their results and obtain estimates of their sensitivity sensitivities and specificites. For both tests, clinicians chose thresholds that yielded high specificity (a low incidence of false-positive results). ECRI's meta-analyses of distal motor latency studies found the sensitivity of the test to be 57% to 66% and the specificity to be 98%. The meta-analysis of palmar sensory latency studies found a sensitivity of 76% and a specificity of 98%.

Figure 16. Distribution of patient ages in studies of surgical treatment for carpal tunnel syndrome



The solid vertical line denotes the mean age for all studies

Figure 17. Sex distribution in surgical trials of surgical treatment for carpal tunnel syndrome

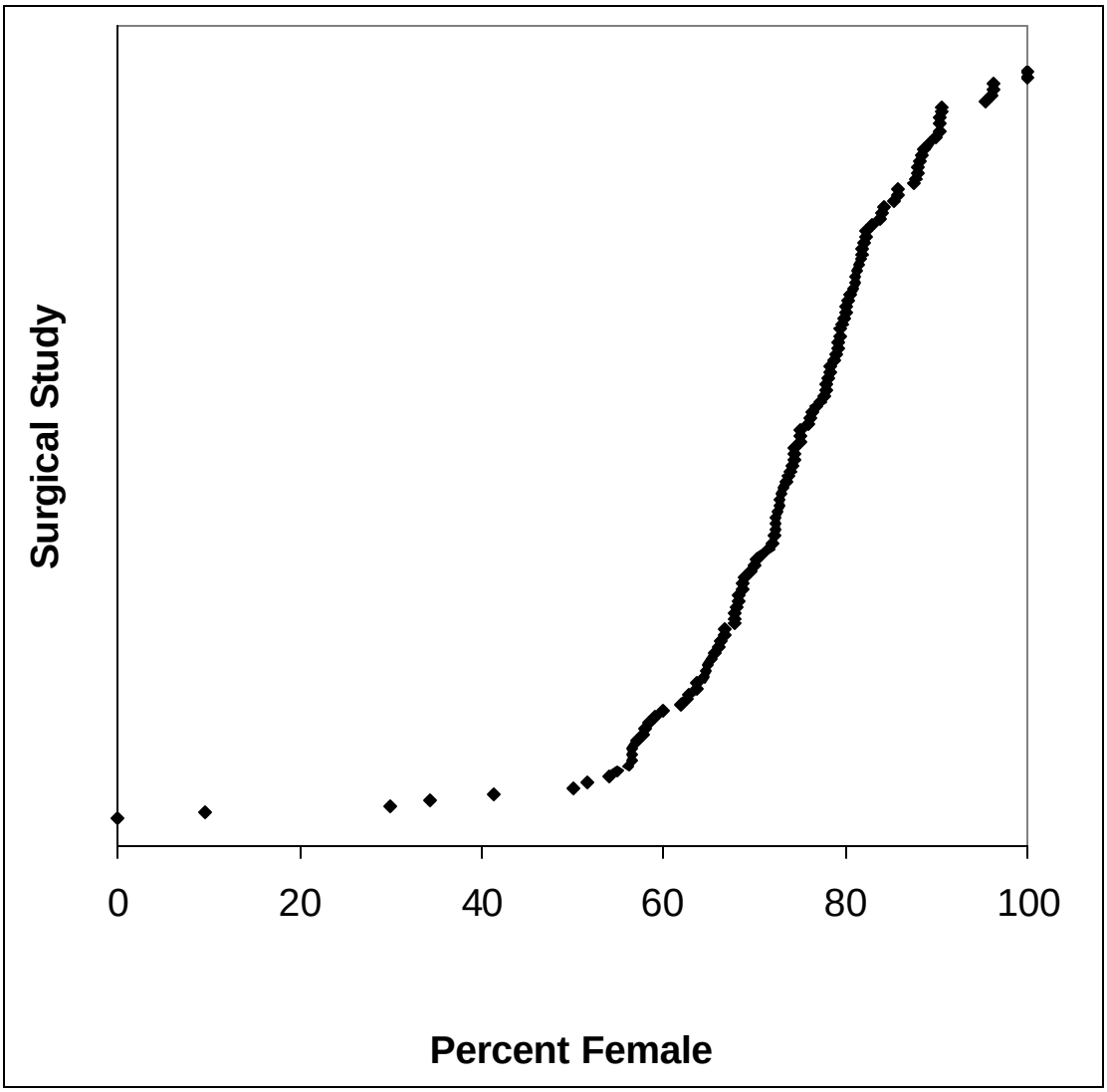
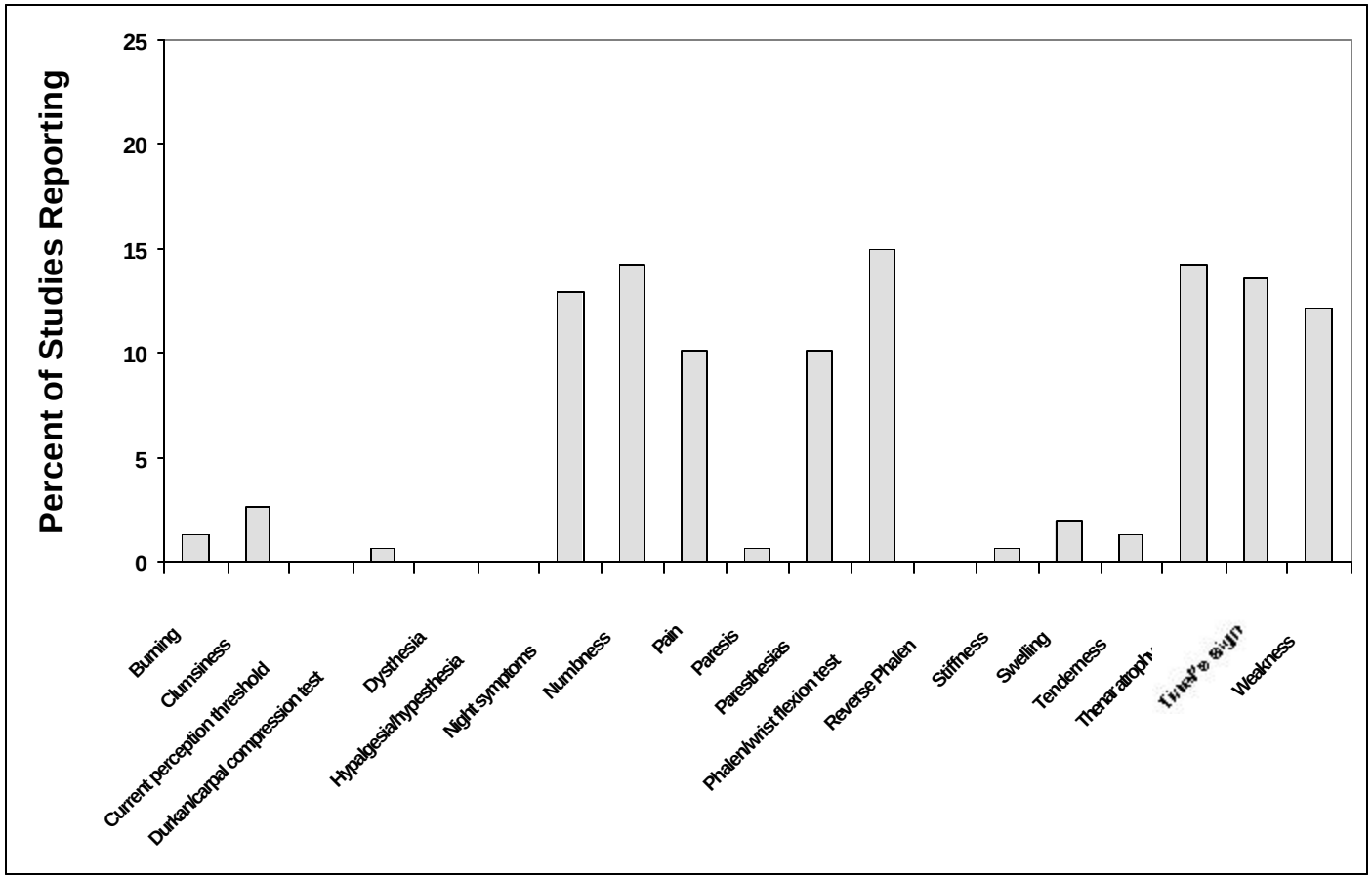


Figure 18. Reporting of symptoms in studies of surgical treatment for carpal tunnel syndrome



Study	Number of patients (or hands)	Sign or symptom	Number of patients with sign or symptom	Percent of patients (or hands)
Palmer, 1993 [397]	173	Weakness	152	87.9%
Waegeneers, 1993 [398]	100 Hands	Weakness	43	43.0%
Pagnanelli, 1992 [400]	456 Hands	Weakness	210	46.1%
Richman, 1989 [412]	12	Weakness	7	58.3%
Kulick, 1986 [418]	167	Weakness	20	12.0%
Freshwater, 1978 [426]	22	Weakness	17	77.3%

Figure 19. Symptoms of patients with carpal tunnel syndrome

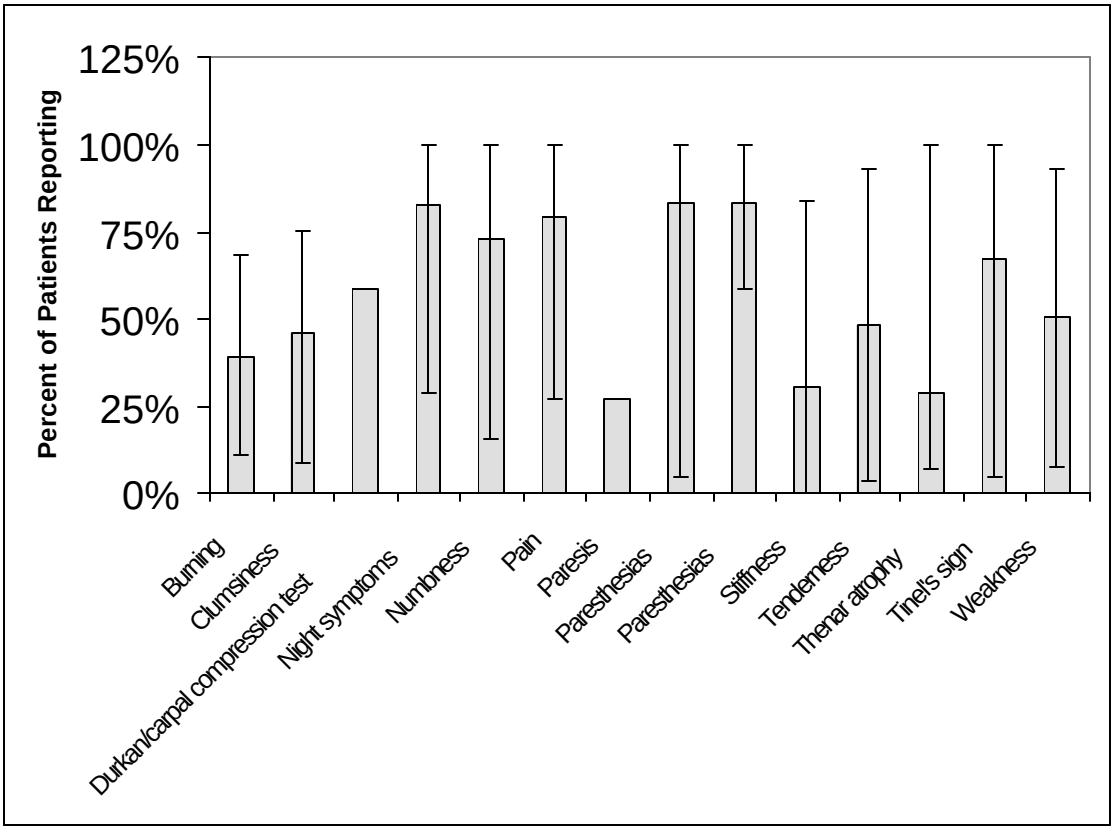
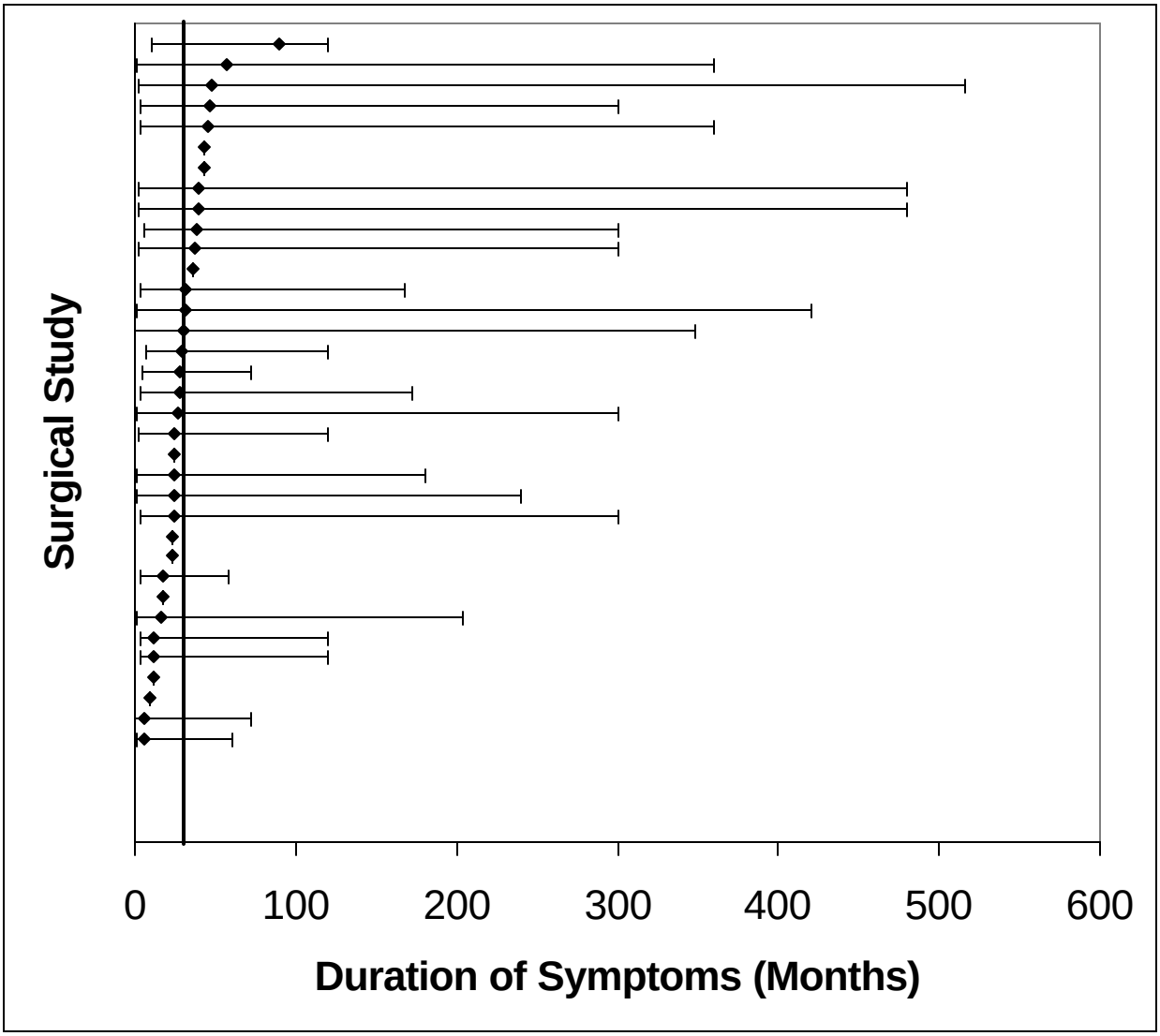


Figure 20. Duration of symptoms in studies of surgery for carpal tunnel syndrome



Solid vertical line denotes the mean duration of symptoms

Figure 21. Number of studies reporting occupations of patients receiving surgery for carpal tunnel syndrome

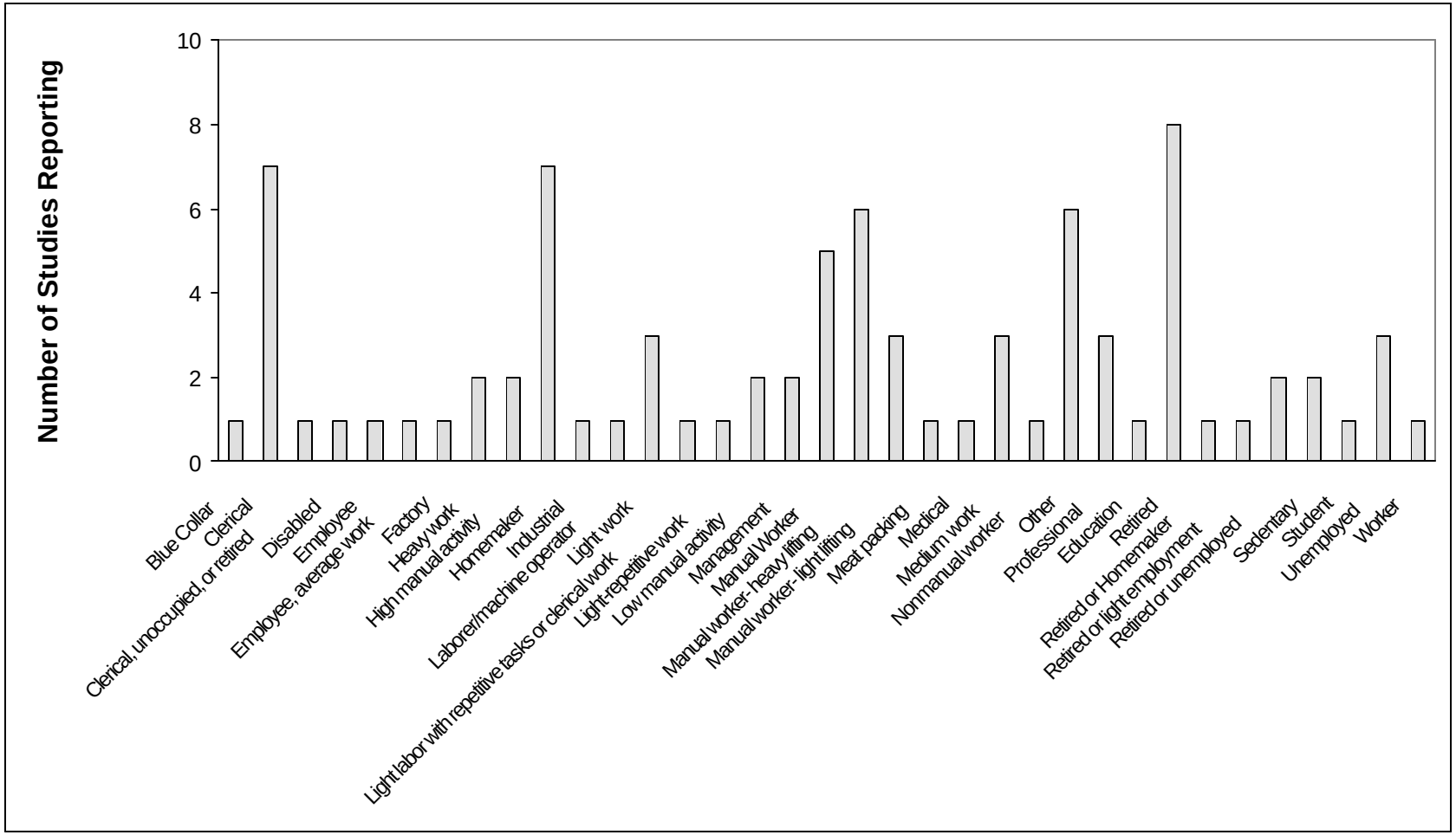


Figure 22. Percent of patients with reported occupations receiving surgery for carpal tunnel syndrome

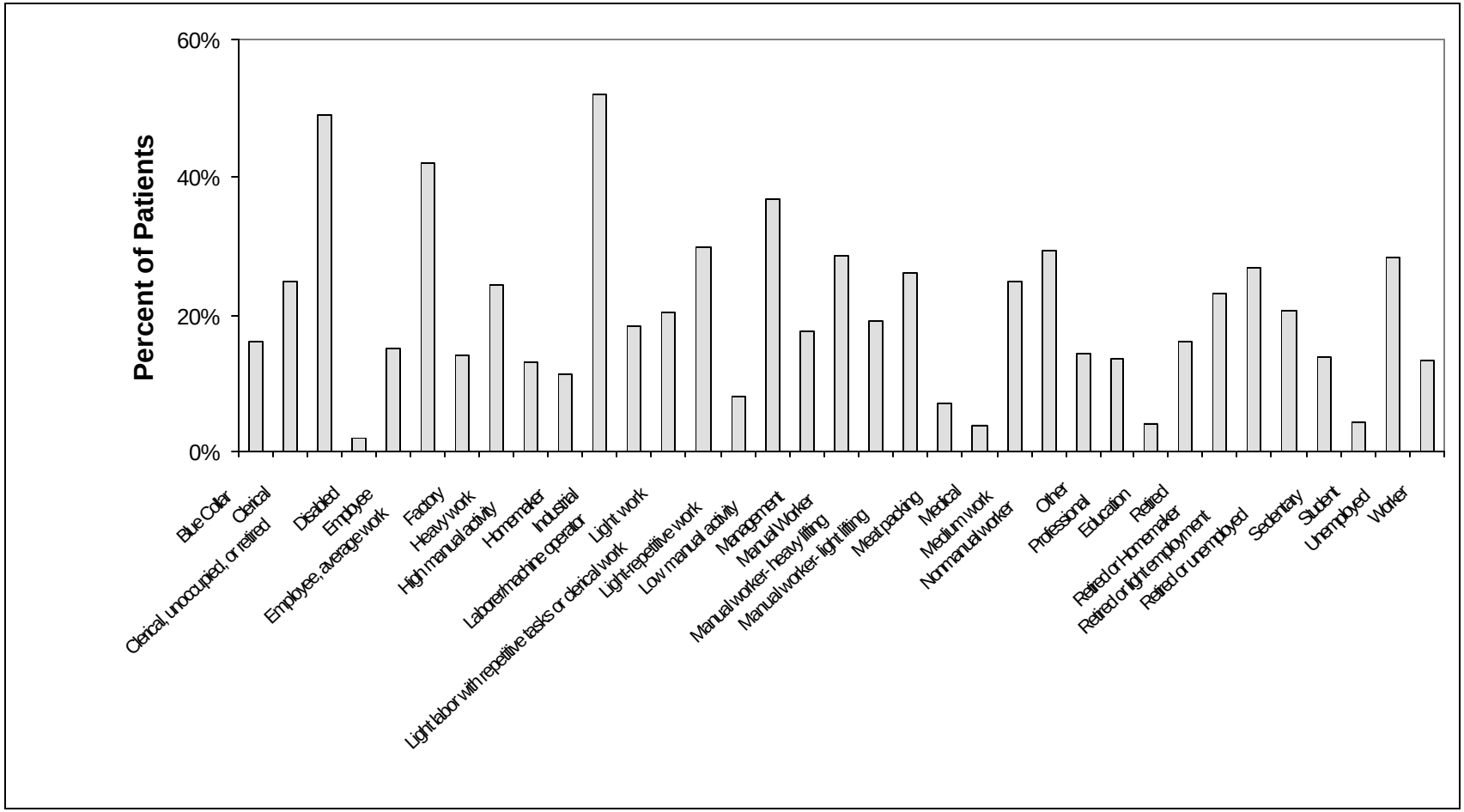


Figure 23. Percent of studies reporting and excluding comorbidities

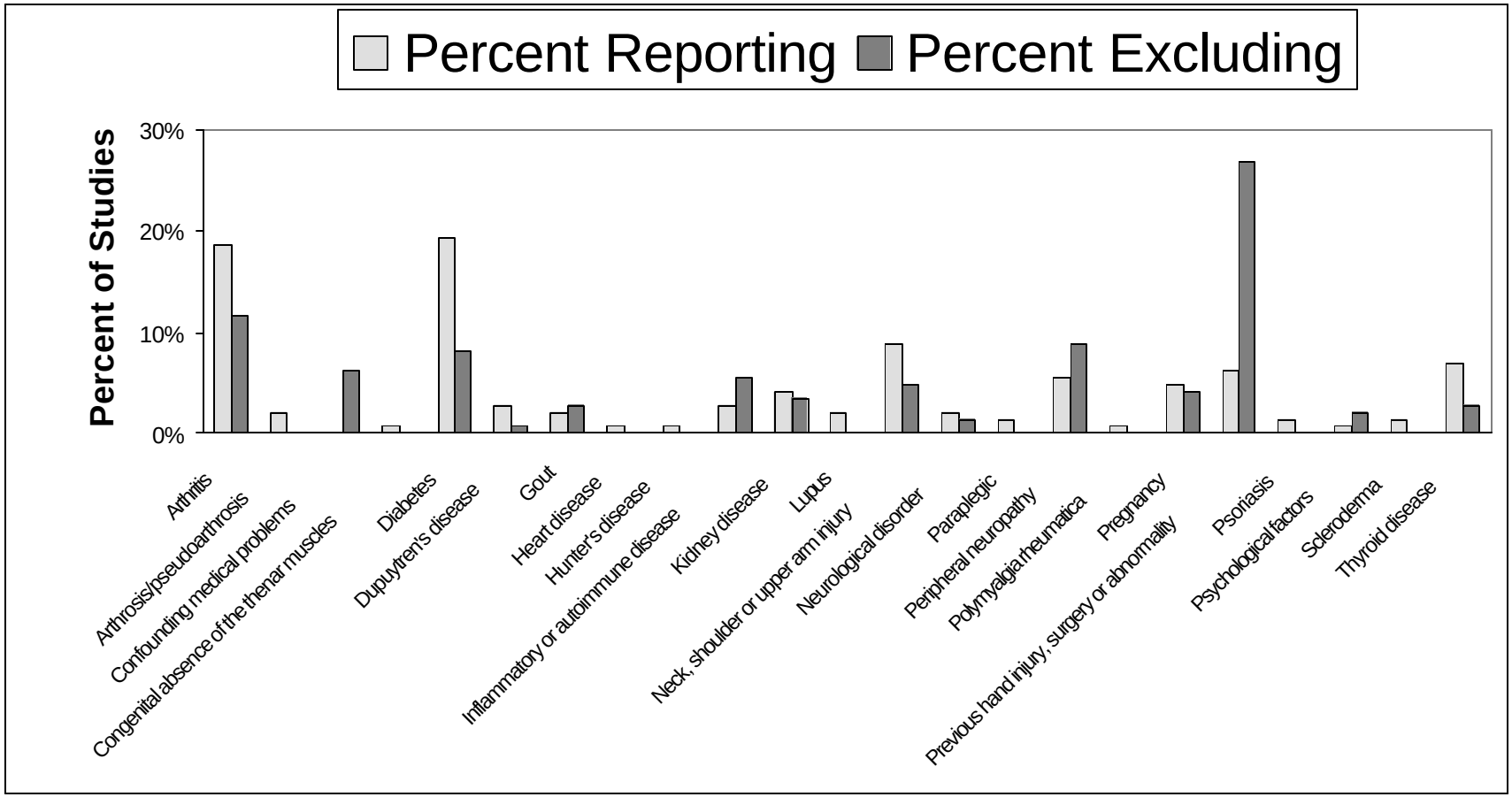


Figure 24. Results of meta-analysis of effect of treatment on global outcome

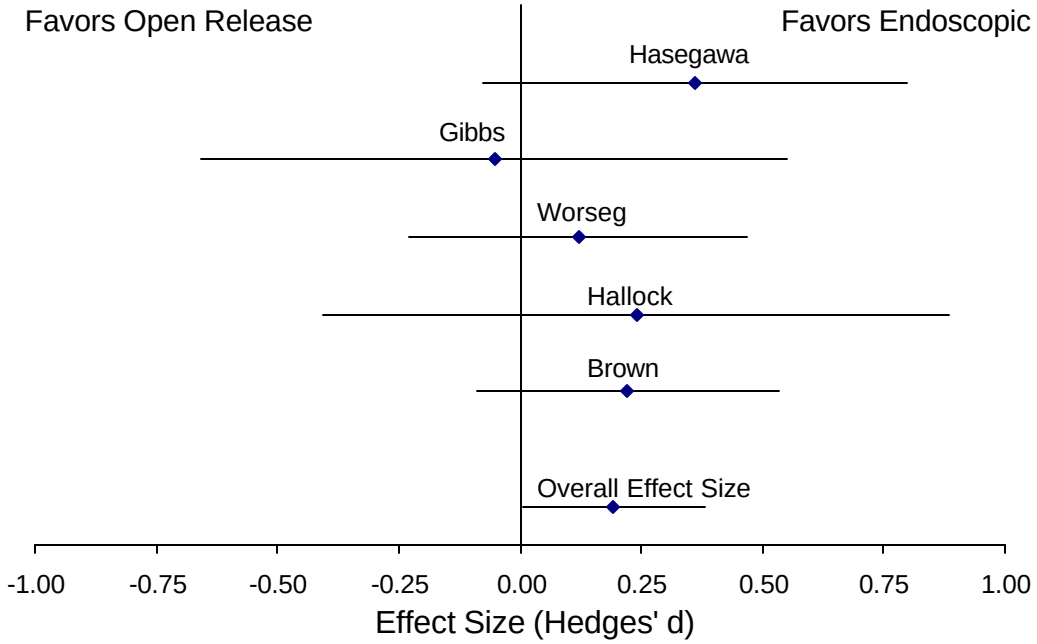


Figure 25. Degree of overlap between outcomes

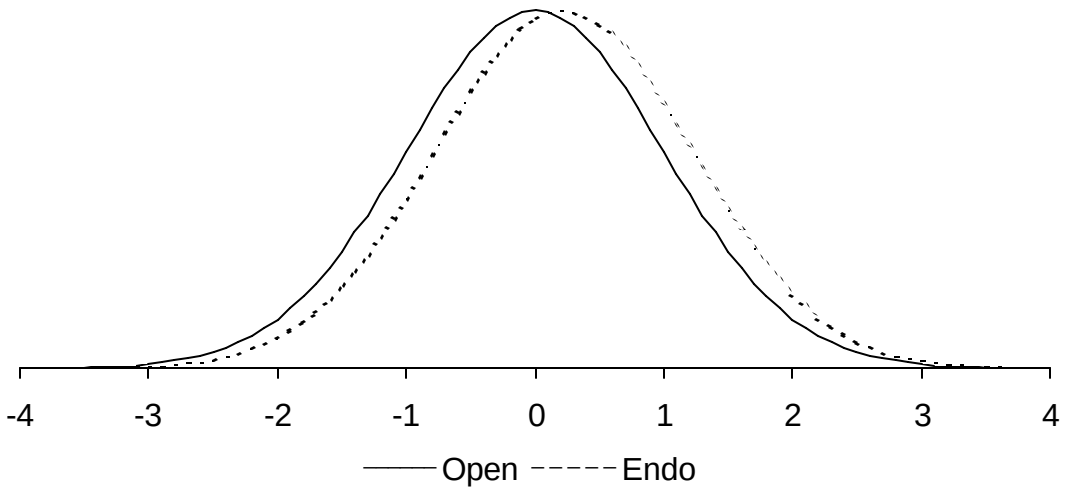
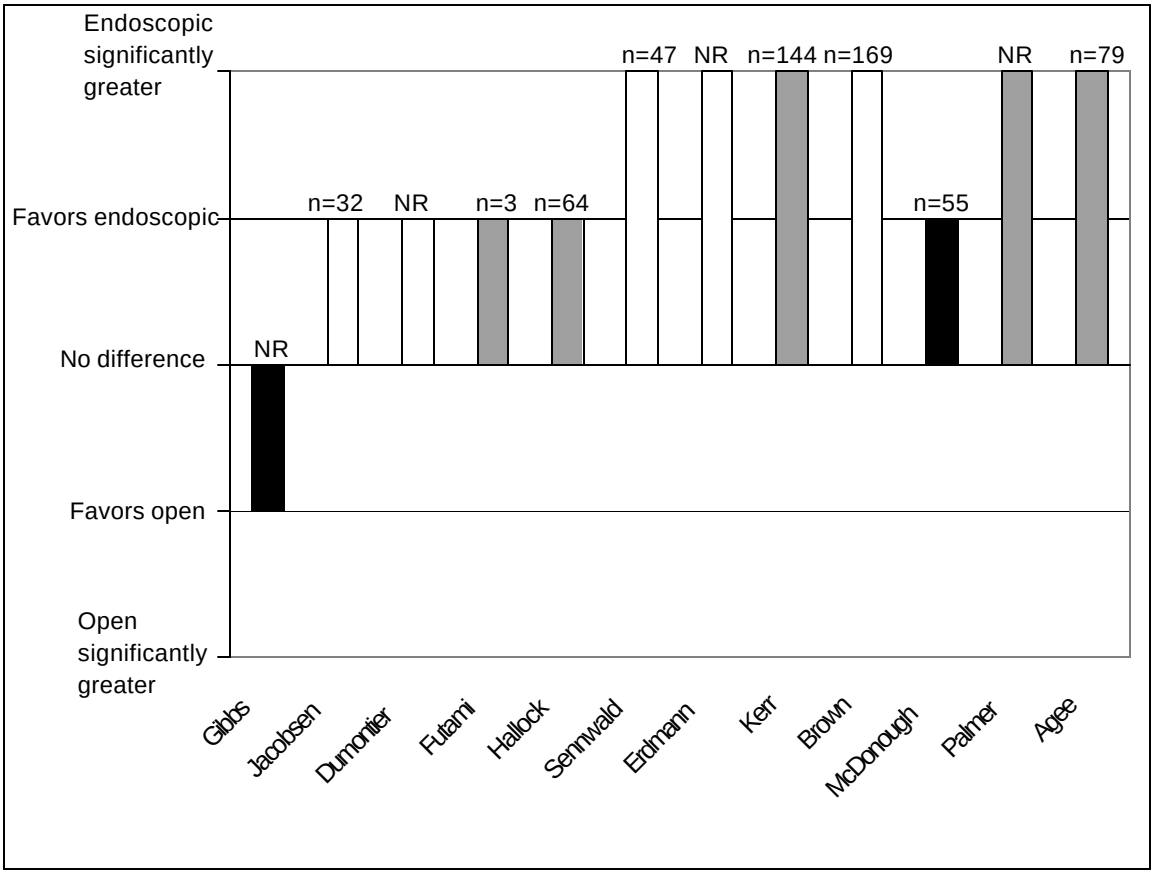
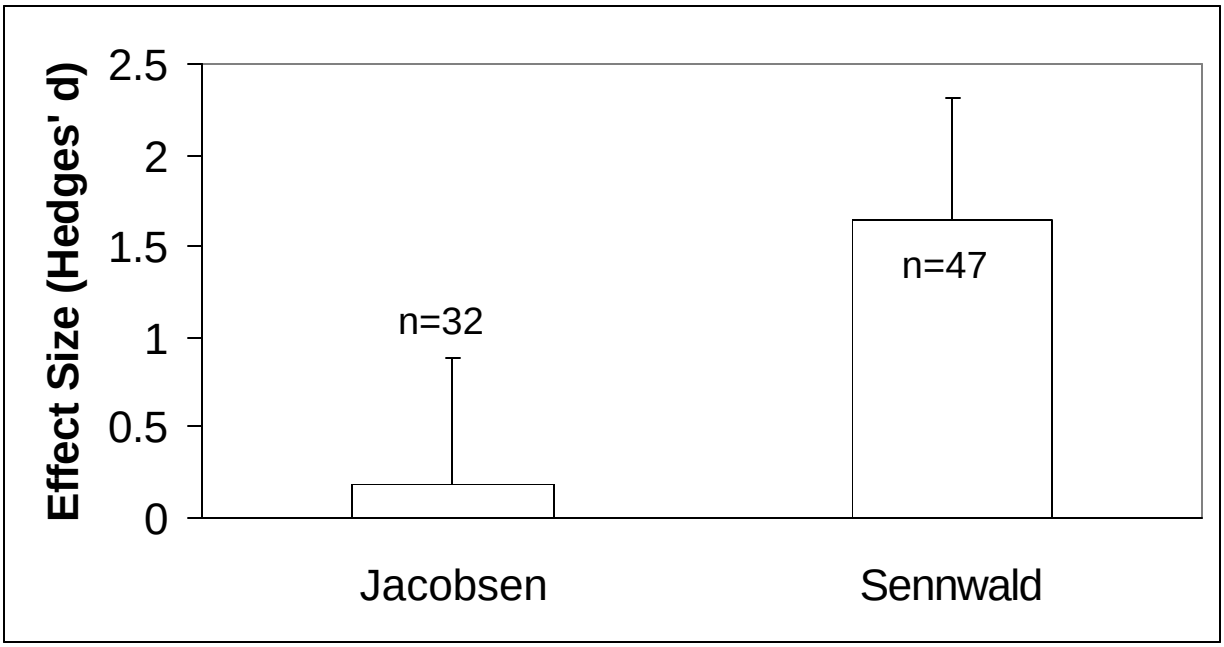


Figure 26. Summary of effect of treatment on return to work



An open bar denotes an RCT, a striped bar a CT, and a filled bar a retrospective trial.
NR indicates that the authors did not report the number of patients for whom this outcome was recorded.

Figure 27. Calculable effect sizes for effect of treatment type on return to work

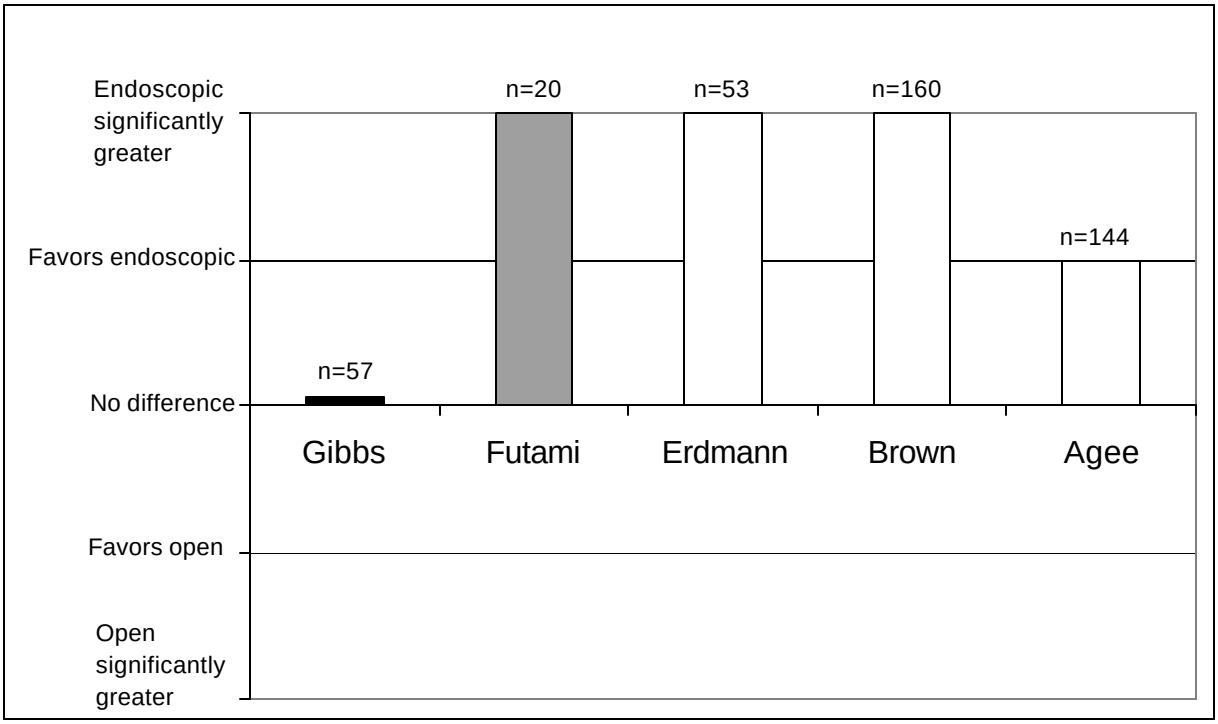


Time to return to activities of daily living

This outcome was reported in five controlled studies, three of which were randomized. Data from these studies are presented in Table 60. Unless otherwise stated, data are presented as mean times to return to activities of daily living (ADLs). Only one study reported sufficient data for a valid effect size to be calculated. Therefore, no meta-analysis could be performed. Instead, Table 61 summarizes trends in the data available from the controlled trials.

Four trials found a faster return to daily activities in the group treated with endoscopic release. Three of these found the difference to be statistically significant. A chi square test conducted by ECRI found that in the study by Brown, the difference between groups at 84 days was statistically significant despite the fact that it was reported as insignificant.[45] The effect size calculated from the same data was significantly different from zero. The study that did not favor endoscopic release was the only retrospective study. It found that both groups returned to daily activities in the same amount of time. This is illustrated in Figure 28.

Figure 28. Summary of effect of treatment on return to ADLs



Open bars represent RCTs, striped bars CTs, and dark bars retrospective trials.

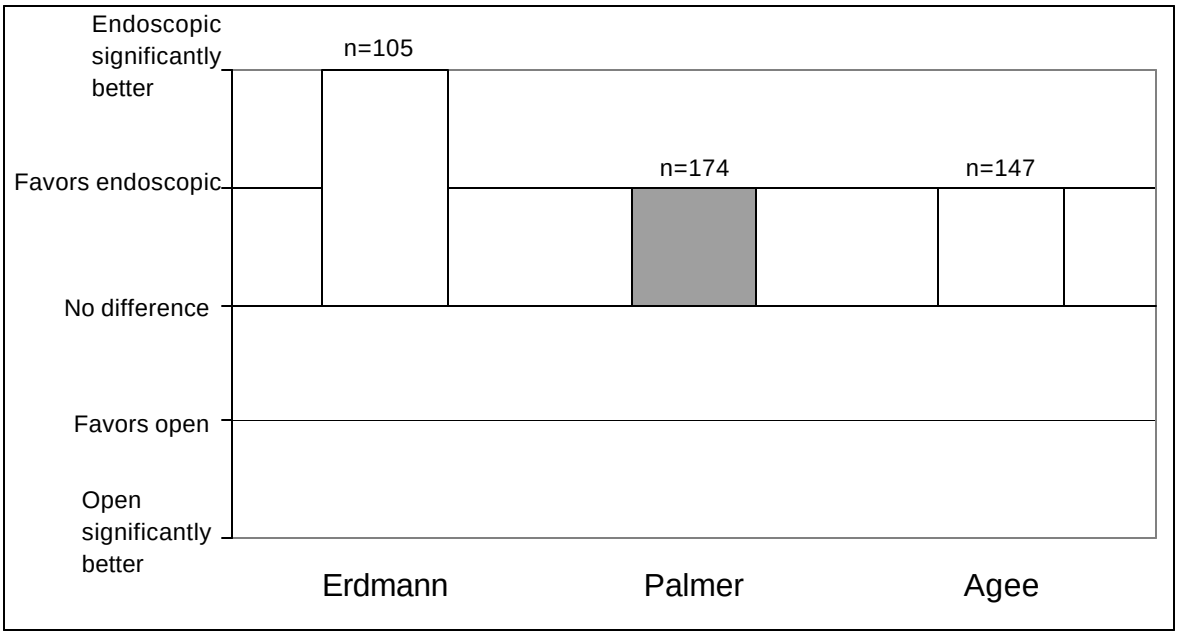
Table 63. Summary of effect of treatment (open or endoscopic) on pain

Study	Which Procedure Had Less Pain?	Was the Difference Stastically Significant?	Power (Minimum percent difference detectable 80% of the time)[a]	Effect Size (95% Confidence Interval)[a]
Gibbs, 1996 [351]	Preop: No difference Early: Not reported Late: Open	Preop: No Early: Not reported Late: No	Preop: 17.5% Early: Not reported Late: 40.0%	Preop: 0.0 (-0.60–0.60) Early: Not reported Late: -0.45 (-1.06-0.15)
Erdmann, 1994 [304]	Preop: Open Early: Endoscopic Late: Endpscopic	Preop: No Early: Yes Late: No	Not calculable	Preop: Not calculable Early: 0.39 (0.00-0.77)[b] Late: Not calculable
Palmer, 1993 [397]	Preop: Endoscopic Early: Endoscopic Late: Endoscopic	Preop: No Early: No Late: No	Not calculable	Not calculable
Agee, 1992 [46]	Preop: Endoscopic Early: Endoscopic Late: Endoscopic	Preop: Not reported Early: Not reported Late: Not reported	Not calculable	Not calculable

a: Calculated by ECRI

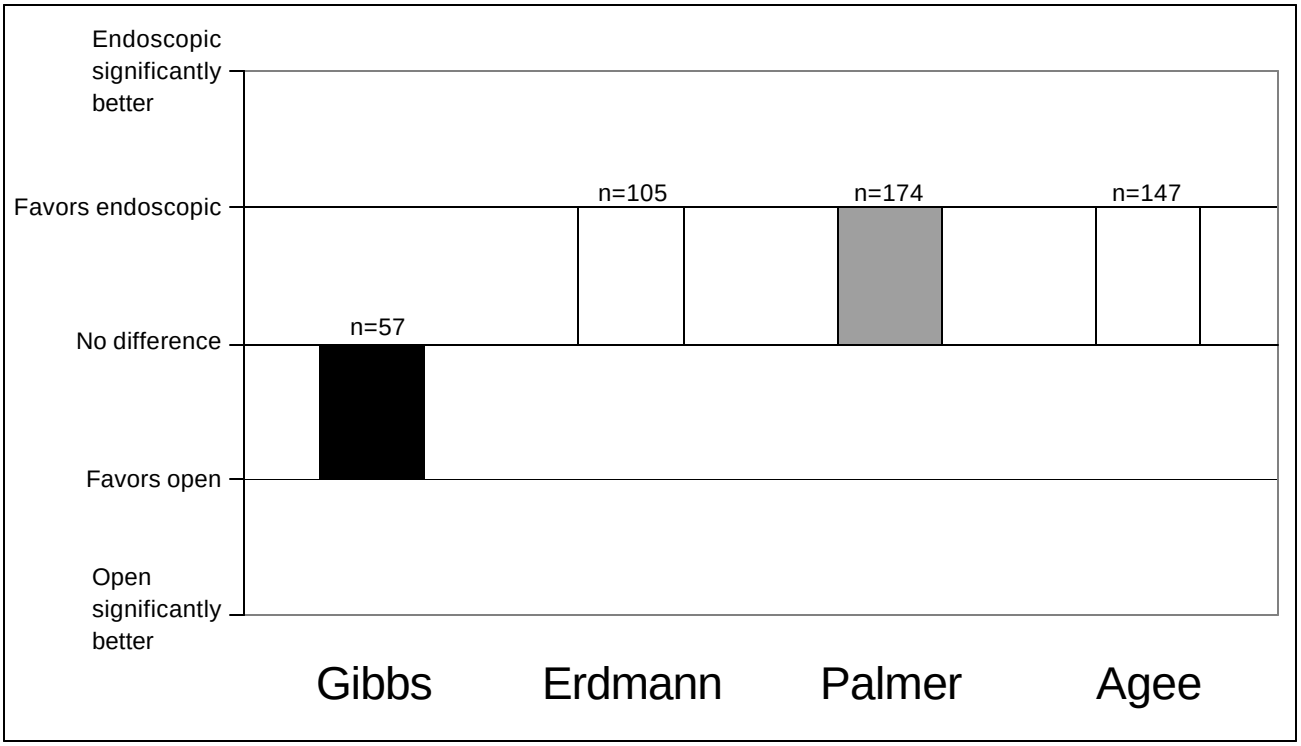
b: Calculated by ECRI based on the conservative assumption that p = 0.049)

Figure 29. Summary of the effect of treatment on pain at early time points



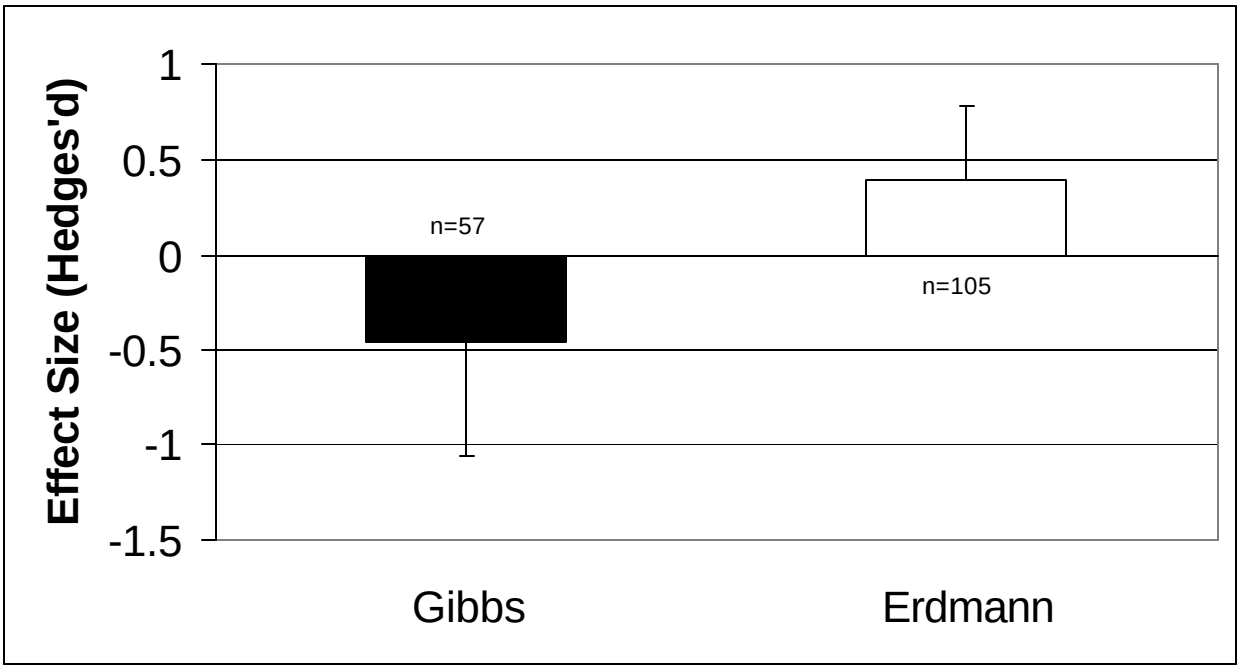
An open bar indicates an RCT, a striped bar a CT. The study by Gibbs does not appear because it did not report early time ponts.

Figure 30. Summary of the effect of treatment on pain at late time points



An open bar indicates an RCT, a striped bar a CT, and a dark bar a retrospective study.

Figure 31. Calculable effect sizes for pain



An open bar indicates an RCT and a dark bar a retrospective study.

Figure 32. Studies reporting minor complications

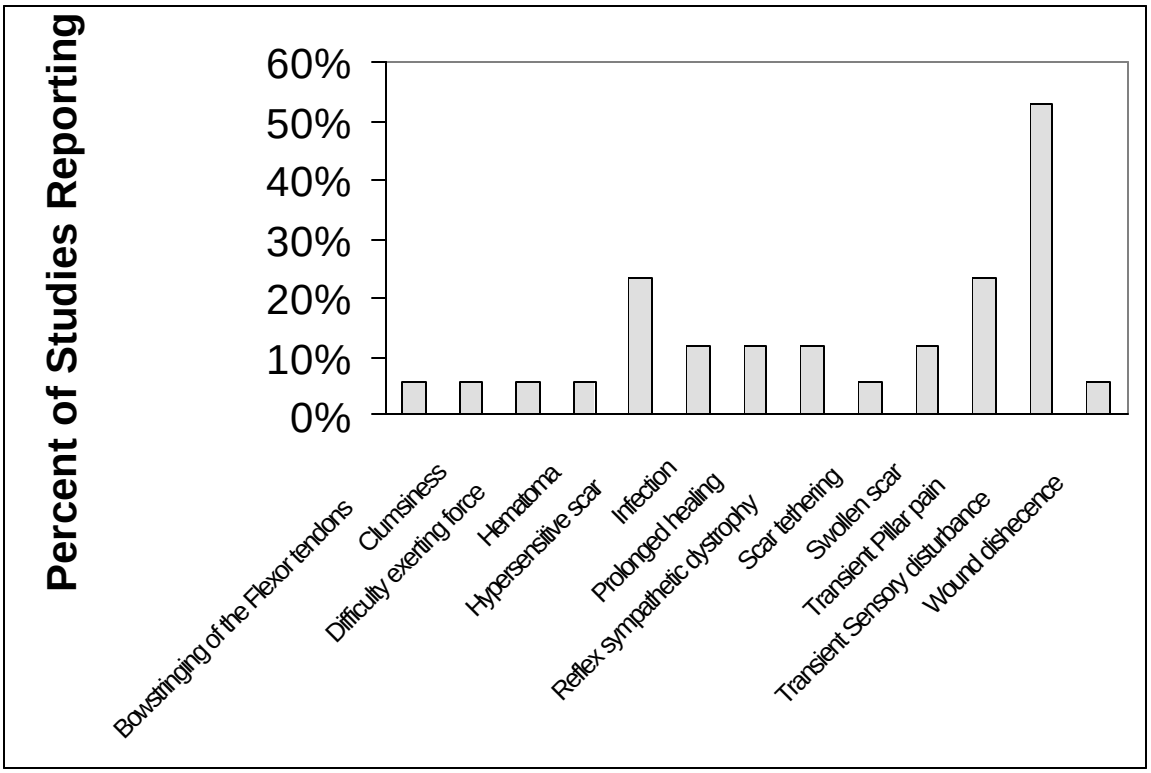


Table 72. Results of conservative meta-analysis of global outcome among patients treated with neurolysis for carpal tunnel syndrome

Author	Year	N	Effect Size	95% CI	p-value	Standardized Residual	Outlier by Std Residual?
Leinberry, [342]	1997	50	0.089	-0.53-0.78	0.778	-0.64	No
Blair, [428]	1996	75	0.067	-1.28-1.42	0.923	-0.30	No
Foulkes, [376]	1994	36	0.432	-0.30-1.17	0.250	0.46	No
Mackinnon, [407]	1991	63	0.282	-0.48-1.04	0.465	0.03	No
Lowry, [429]	1988	50	0.140	-0.41-0.70	0.615	-0.52	No
Gelberman, [415]	1987	61	0.697	0.11-1.28	0.019	1.61	No
Holmgren, [416]	1987	41	-0.741	-2.04-0.56	0.263	-1.56	No
Freshwater, [426]	1978	26	0.324	-1.08-1.72	0.650	0.08	No
			Fixed effects model:				
			Overall Effect Size	95% CI	p-value of E.S.	Q	p-value of Q
			0.27	0.003-0.537	0.047	5.20	0.636

Figure 33. Results of meta-analysis of the effect of neurolysis on global outcome

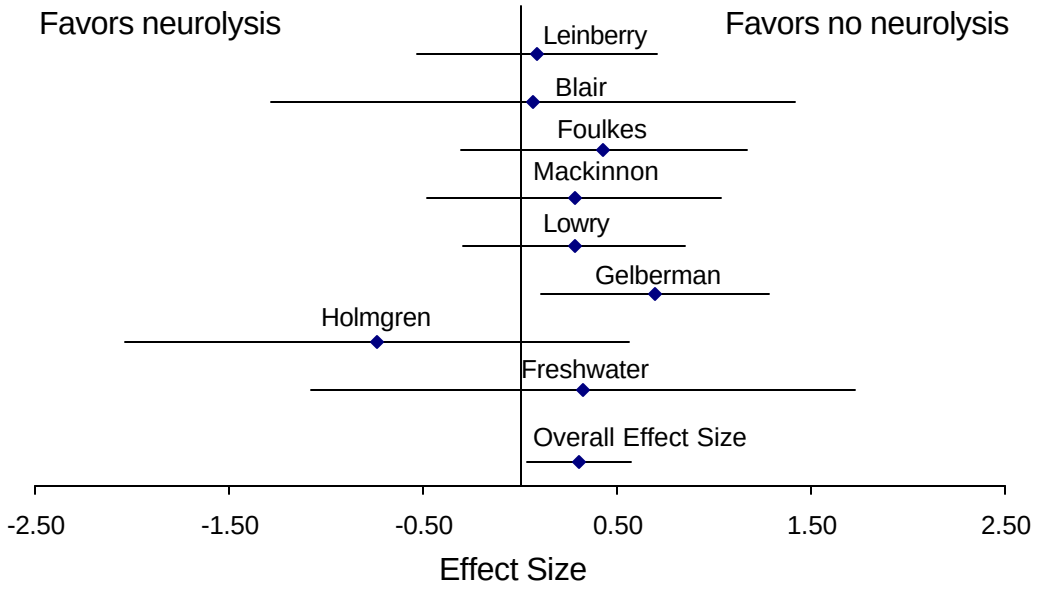


Figure 34. Overlap between effects of neurolysis and no neurolysis

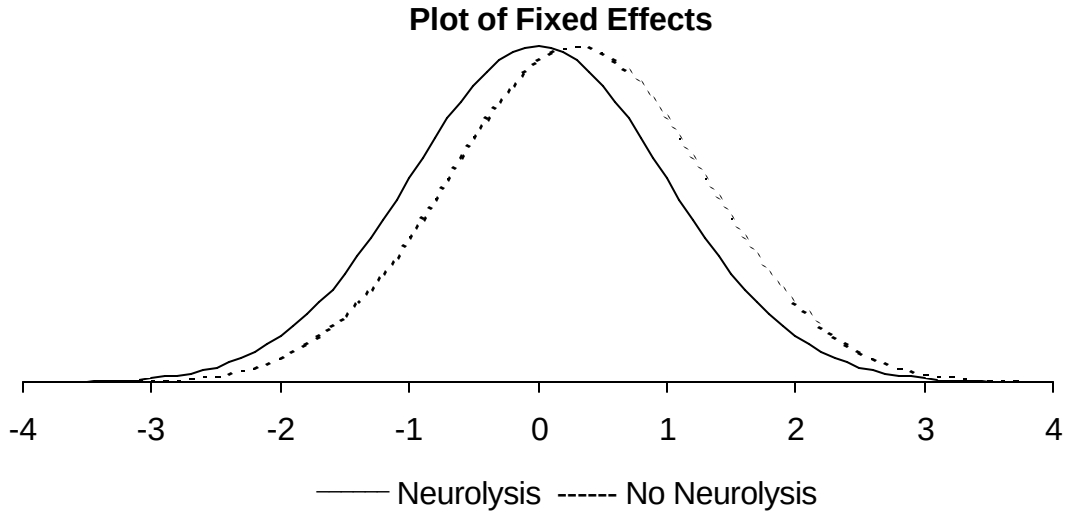
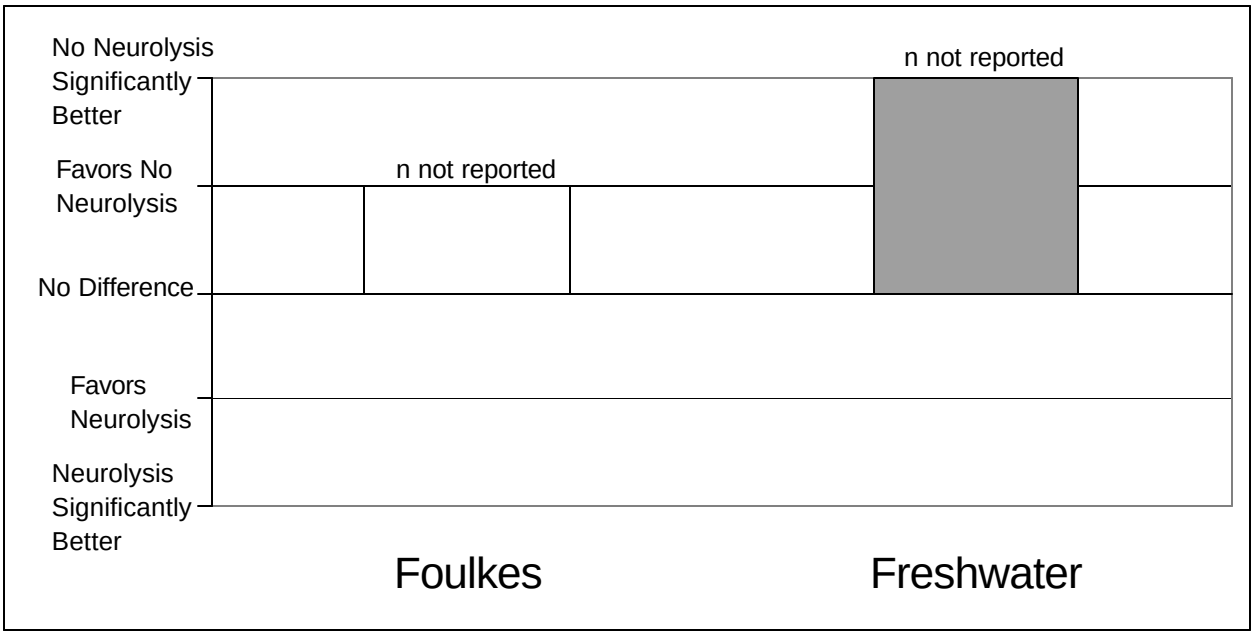


Figure 35. Summary of the effect of neurolysis on return to work



An open bar indicates an RCT, while a striped bar indicates a CT.

Return to Activities of Daily Living

No studies reported this outcome.

Pain

Three controlled trials, two of which were randomized, compared pain in patients who received surgery with and without neurolysis. Results are presented in Table 77. The study by Freshwater and Arons found no statistically significant differences between groups in incidence of night pain and tenderness.[426] Too few patients (6, or 23%) had wrist pain prior to treatment for any statistical analysis of differences in pain between groups to be made. The study by Blair shows a trend toward superior results from neurolysis, but the difference between groups is not significant (chi square test conducted by ECRI, p = 0.106). Given the 36% loss to followup in the study, as discussed above, its results are not conclusive. If only the more successful candidates returned for followup, this would bias the results. Holmgren-Larssen et al.[433] found that the patients treated with neurolysis had a resurgence in pain at 6-month followup, while the patients with no neurolysis did not. The statistical significance of this trend cannot be determined, however, because they did not report the number of patients in each group.

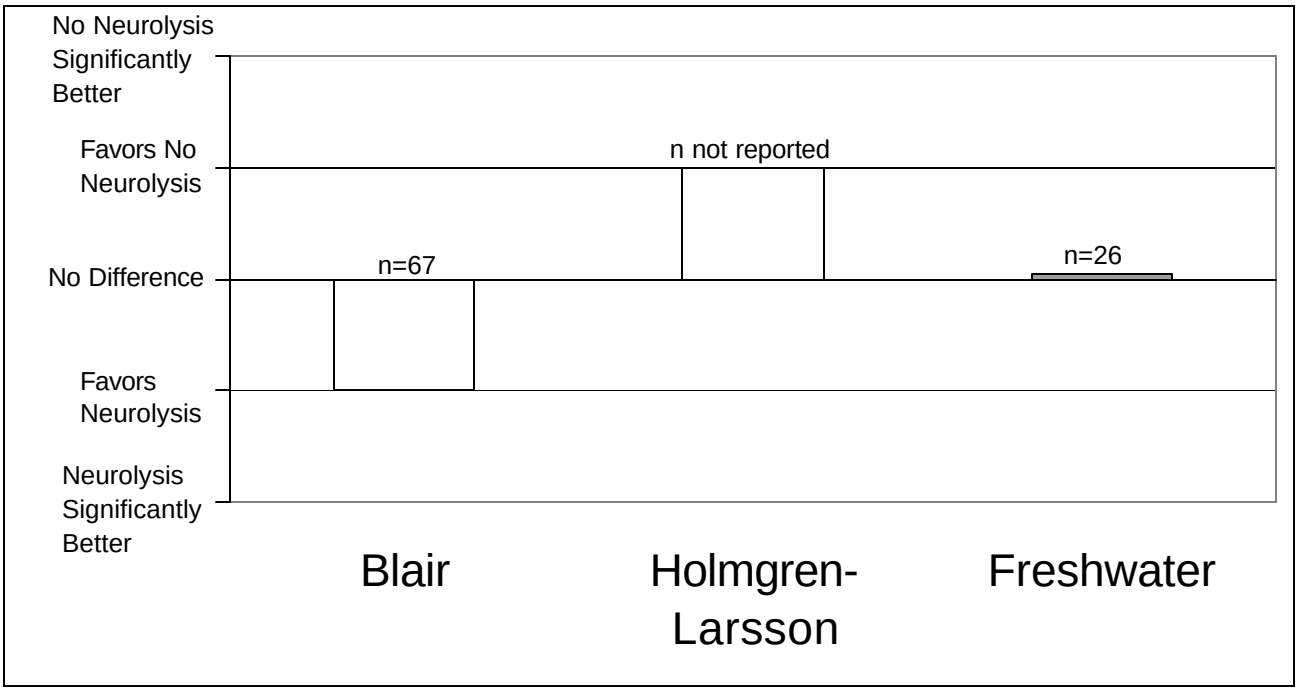
These results are summarized in Table 78 and Figure 36. Calculable effect sizes are presented in Figure 37. The available data are of insufficient quality and quantity to allow one to reach n evidence-based conclusion about whether there is a difference in symptomatic pain resulting from performing or not performing neurolysis.

Table 78. Summary of the effect of neurolysis on pain

Study	Which Procedure led to less pain?	Was the Difference Stastically Significant?	Power (Minimum percent difference detectable)[a]	Effect Size (95% Confidence Interval)[a]
Blair, 1996 [428]	Neurolysis	No	28%	-0.57 (-1.23-0.10)
Holmgren-Larsson, 1985 [433]	No Neurolysis	No	Not calculable	Not calculable
Freshwater, 1978 [426]	No difference	No	Not calculable	0.08 (-2.12-2.28)

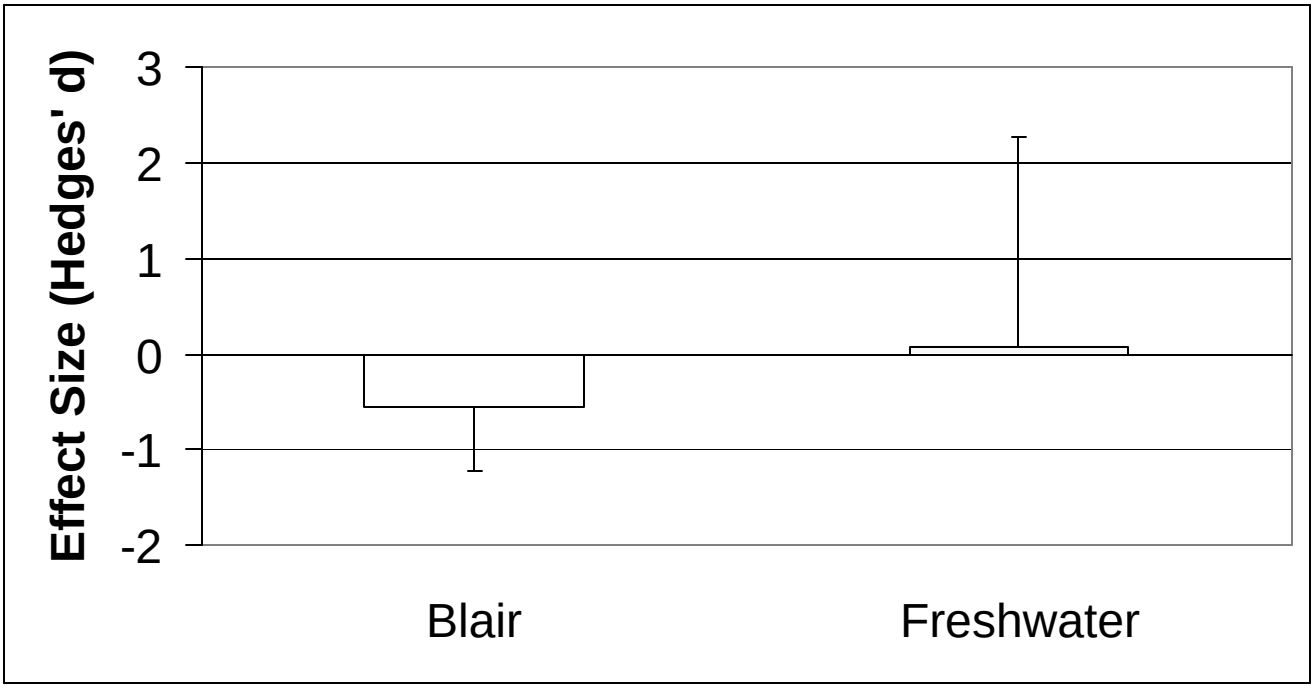
a: Calculated by ECRI

Figure 36. Summary of effect of neurolysis on pain



An open bar indicates an RCT, a striped bar indicates a CT.

Figure 37. Size of effect (Hedges' d) of neurolysis on pain



Function

Two randomized controlled trials of carpal tunnel release with or without neurolysis reported measures of function. Both included patients treated for bilateral CTS, and both had high (36%-50%) rates of attrition. Their results can be found in Table 79. Foulkes et al. asked patients to rate their hand function on a scale of 0-100, while Blair et al. reported the number of patients having difficulty in three specific activities. As can be seen in Table 80 and Figure 38, neither study found a statistically significant difference between groups, and no clear trends can be observed favoring one group or the other. Differences between groups are small, and, in the case of Blair, would have to be large (at least 44%) before the study would have the statistical power to find them significant.

Table 80. Summary of effect of neurolysis on hand function

Study	Which Procedure led to superior function?	Was the Difference Stastically Significant?	Power (Minimum percent difference detectable)[a]	Effect Size (95% Confidence Interval)
Blair, 1996 [428]	Neurolysis	No	Screwing Lids: 62% Picking up objects: 57% Lifting: 44%	Not calculable
Foulkes, 1994 [376]	Open release	Not reported	Not calculable	Not calculable

a: Calculated by ECRI

Figure 38. Summary of effect of neurolysis on hand function

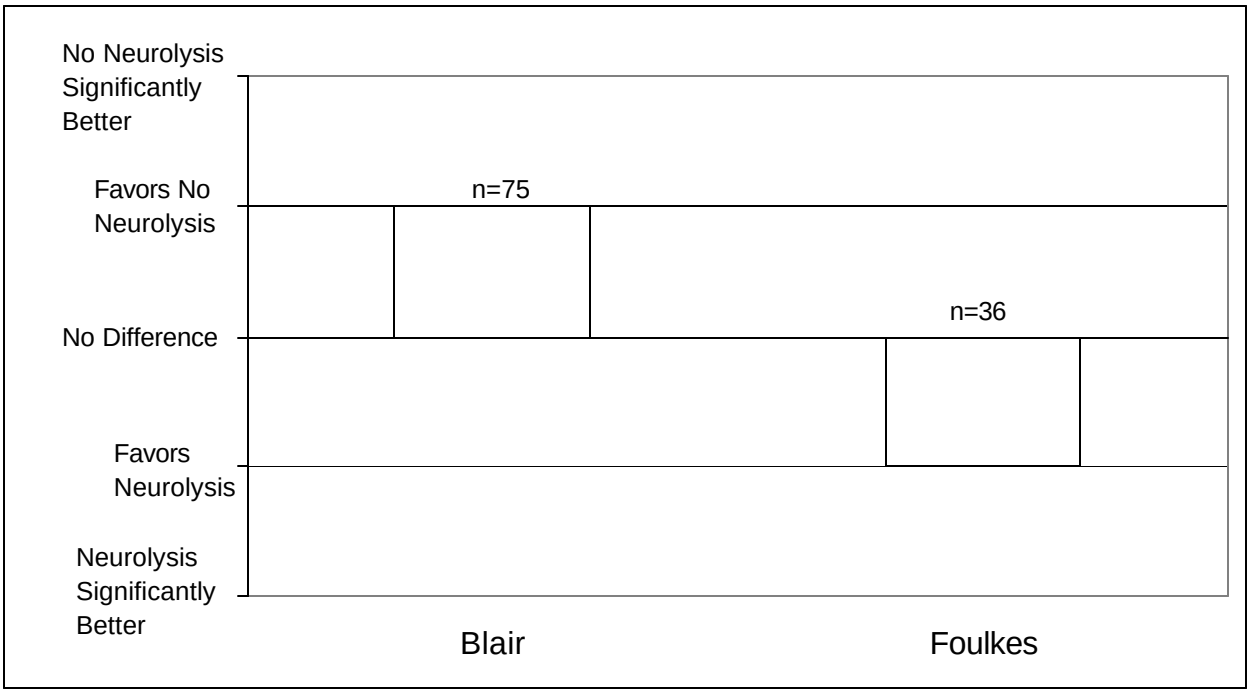
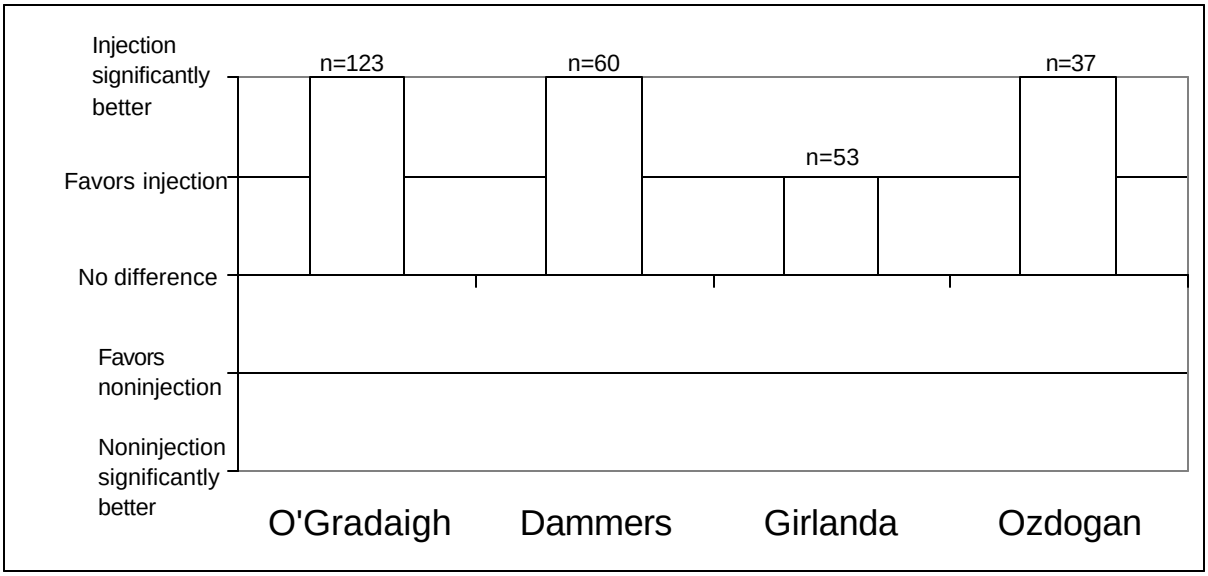


Figure 39. Summary of effect of injection on global outcome



Return to Work

No studies reported this outcome.

Return to Activities of Daily Living

No studies reported this outcome.

Pain

No studies reported this outcome.

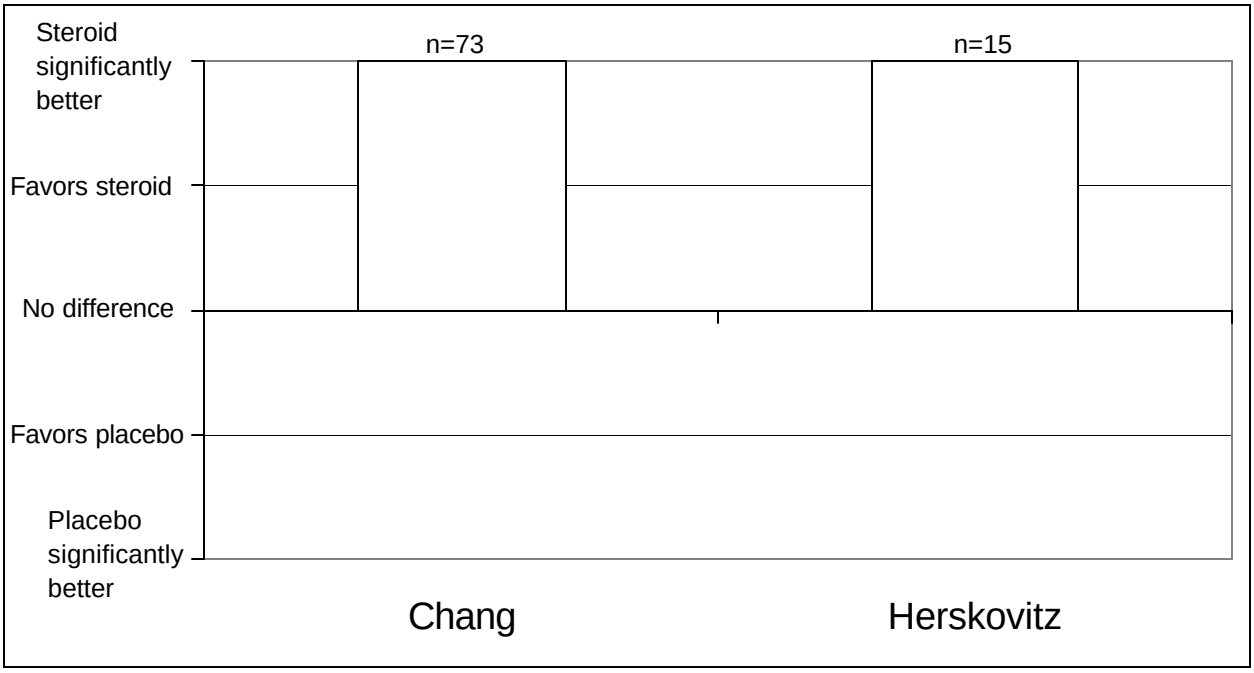
Function

No studies reported this outcome.

Quality of Life

No studies reported this outcome.

Figure 40. Summary of effect of oral steroids on global outcome



Return to Work

Neither study reported this outcome.

Return to Activities of Daily Living

Neither study reported this outcome.

Pain

Because the study by Chang did not report this outcome, only the effect of oral steroids can be considered. Herskovitz et al. reported that improvement in pain scores was significantly greater in the steroid group than the control ($p = 0.07$, 0.03 and 0.008 at 2, 4, and 8 weeks, respectively by t-test). Because the raw were not reported, no analysis is possible. Although the differences may be statistically significant, without information regarding their magnitude (effect size), we are unable to determine whether they are clinically significant. Further, the results of a single small trial are insufficient evidence for conclusions to be drawn.

Function

Neither study reported this outcome.

Table 122. Summary of effect of splinting after surgery on global outcome

Study	Which Procedure led to Superior Global Outcome?	Was the Difference Stastically Significant?	Power (Minimum percent difference detectable)[a]	Effect Size (95% Confidence Interval)[a]
Bury, 1995 [364]	No Splint	No	Number symptom-free 28% Categorical rating[b] 29%	Number symptom-free 0.06 (-0.61 – 0.72) Categorical rating[b] 0.89 (-0.78-2.56)
Cook, 1995 [432]	No Splint	Yes	Not calculable	14 Days 0.38 (-0.18-0.94) 1 Month 0.86 (0.28-1.44)

a: Calculated by ECRI

b: Calculated by ECRI by collapsing the categorical rating into a dichotomous one: number cured or improved.

Figure 41. Effect of splinting after surgery on global outcome

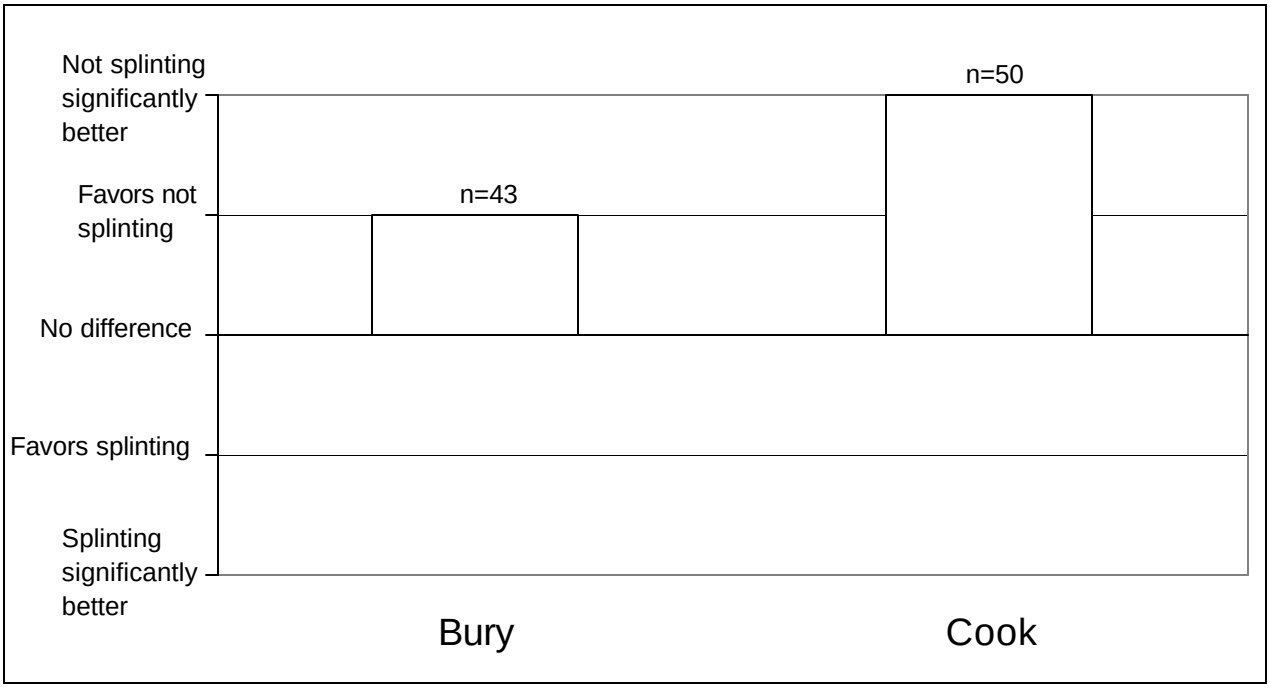
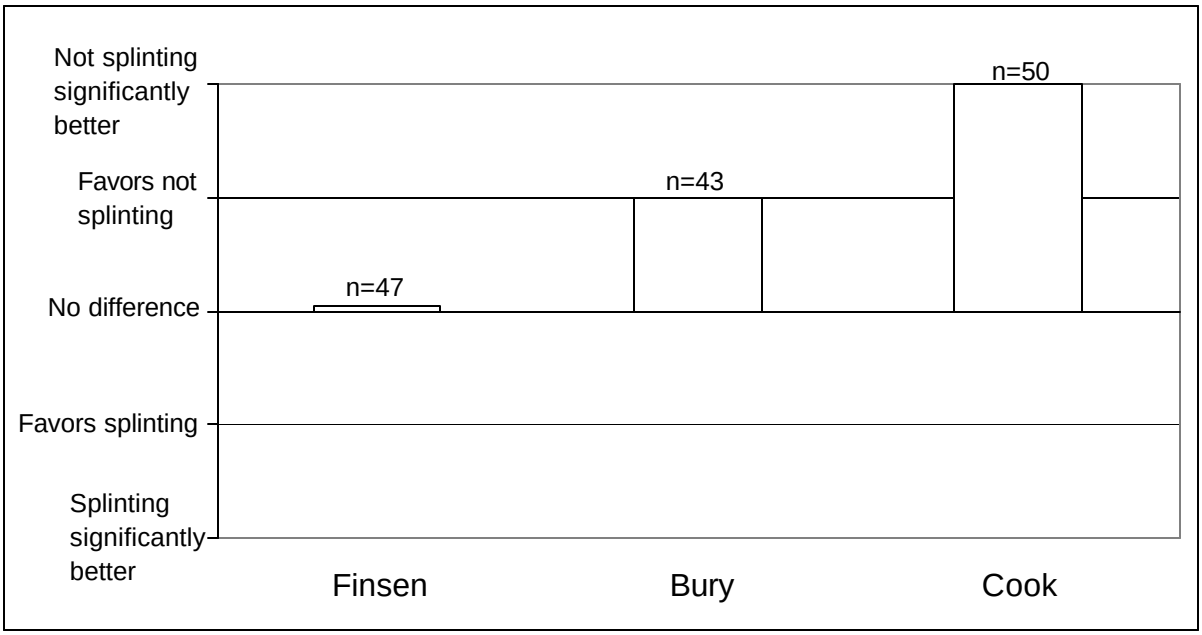


Table 124. Summary of effect of splinting after surgery on return to work

Study	Which Procedure led to Superior Outcome?	Was the Difference Stastically Significant?	Power (Minimum percent difference detectable)[a]	Effect Size (95% Confidence Interval)[a]
Finsen, 1999 [319]	No difference	No	Not calculable	Not calculable
Bury, 1995 [364]	No Splint	No	24%	0.55 (-0.39 – 1.49)
Cook, 1995 [432]	No Splint	Yes	Not calculable	Light duty: 0.75 (0.17 – 1.32) Full duty: 0.82 (0.24-1.40)

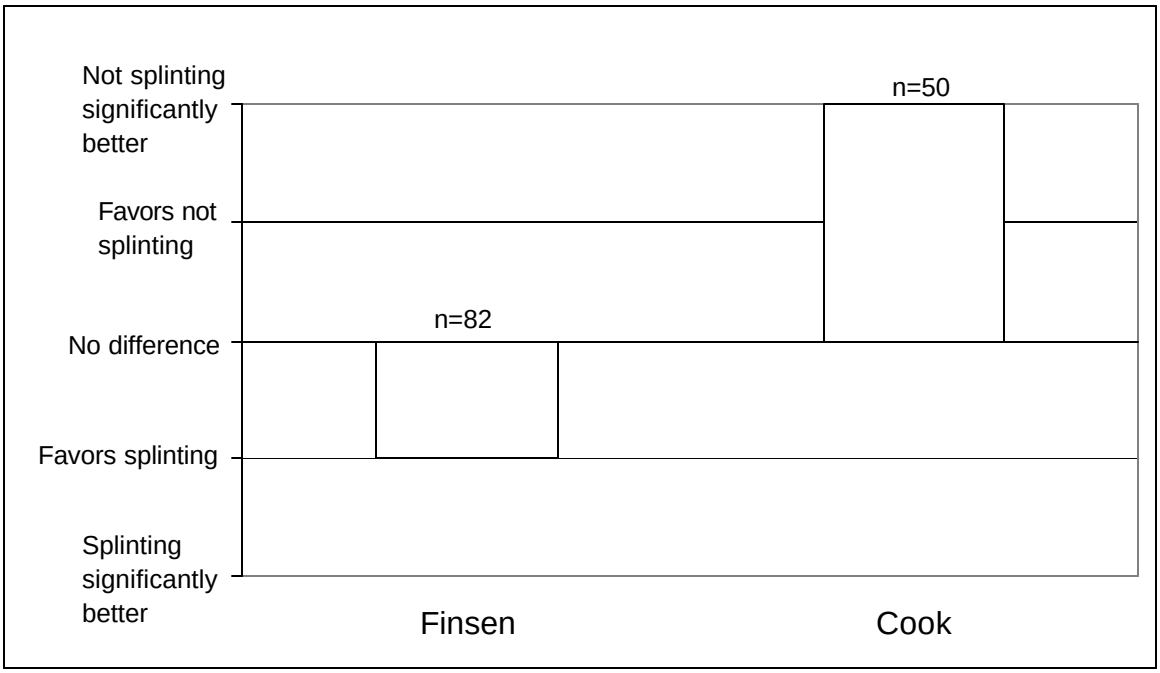
Figure 42. Effect of splinting after carpal tunnel surgery on return to work



Return to Activities of Daily Living

One study of 50 patients reported on time to return to activities of daily living. The results are presented in Table 125. These results show a statistically significant advantage to not splinting.[432] The effect size is significantly different from zero (d = 1.06, 95%C.I. 0.47 – 1.65).

Figure 43. Summary of effect of splinting after surgery on pain



Harms

All three studies reported harms, but as listed in Table 128, none reported the same harms. Although all reported harms occurred in the unsplinted group, both the numbers of patients and the numbers of harms are too small to demonstrate significant differences between groups. No evidence-based conclusions can be drawn as to whether splinting after surgery prevents complications.