CLINICAL PRACTICE GUIDELINES

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Hand Pain and Sensory Deficits: Carpal Tunnel Syndrome

Clinical Practice Guidelines
Linked to the International Classification of Functioning, Disability, and Health
from the Academy of Hand and Upper Extremity Physical Therapy and the Academy of Orthopaedic Physical Therapy of the American Physical Therapy Association

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HAND PAIN AND SENSORY DEFICITS – CARPAL TUNNEL SYNDROME: CLINICAL PRACTICE GUIDELINES 2019

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SUMMARY OF RECOMMENDATIONS

Classification

Differential Diagnosis (Provocative Tests)

Differential Diagnosis (Sensory Measures)

Combined Testing

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Interventions: Manual Therapy Techniques

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Manual Therapy

Interventions: Therapeutic Exercise

Stretching

*These recommendations and clinical practice guidelines are based on the scientific literature accepted for publication prior to November 2018.

LIST OF ACRONYMS

2PD: 2 point discrimination
+LR: positive likelihood ratio
-LR: negative likelihood ratio
APB: abductor pollicis brevis
APTA: American Physical Therapy Association
BMI: body mass index
CI: confidence interval
CMAP: compound muscle action potential
CPG: clinical practice guideline
CTQ-6: 6 item version of the CTQ-SSS
CTQ-FS: Boston Carpal Tunnel Questionnaire Functional Scale
CTQ-SSS: Boston Carpal Tunnel Questionnaire Symptom Scale Severity
CTR: carpal tunnel release
CTS: carpal tunnel syndrome
DASH: Disabilities of the Arm, Shoulder and Hand
DIP: distal interphalangeal
DM: diabetes mellitus
DML: distal motor latency
DSL: distal sensory latency
DMPUT: Dellon-modified Moberg pick-up test
ES: effect size
FDS: flexor digitorum superficialis
FDP: flexor digitorum profundus
FPL: flexor pollicis longus
HR: hazard ratio
ICC: intraclass correlation coefficient
ICD: International Classification of Diseases
ICF: the World Health Organization's International Classification of Functioning, Disability and Health
IFC: interferential current
LDL:
MCID: minimal clinically important difference
MD: mean difference
MP: metacarpalphalangeal
NCS: nerve conduction studies
NCV: nerve conduction velocity
NPV: negative predictive value
OR: odds ratio
PIP: proximal interphalangeal
PPB: Purdue pegboard
PPV: positive predictive value
QuickDASH: 11 item version of the DASH
RCT: randomized controlled trial
SNAP: sensory nerve action potential
SNCV: sensory nerve conduction velocity
SRM: standardized response mean
SSCT: subsynovial connective tissue

SWMT: Semmes Weinstein monofilament testing
TENS: transcutaneous electrical nerve stimulation
ULNT: upper limb neurodynamic test
US: ultrasound
VAS: visual analog scale

AIM OF THE GUIDELINES

The Academy of Hand and Upper Extremity Physical Therapy and Academy of Orthopaedic Physical Therapy of the American Physical Therapy Association (APTA) have an ongoing effort to create evidence-based practice guidelines for management of patients with musculoskeletal impairments described in the World Health Organization's International Classification of Functioning, Disability, and Health (ICF).[297]

The purposes of these clinical guidelines are to:

- Describe evidence-based practice including diagnosis, prognosis, intervention, and assessment of outcome for musculoskeletal disorders
- Classify and define common musculoskeletal conditions using the World Health Organization's terminology related to impairments of body function and body structure, activity limitations, and participation restrictions
- Identify interventions supported by current best evidence to address impairments of body function and structure, activity limitations, and participation restrictions associated with common musculoskeletal conditions
- Identify appropriate outcome measures to assess changes resulting from physical therapy interventions in body function and structure as well as in activity and participation of the individual
- Provide a description to policy makers, using internationally accepted terminology, of the practice of orthopaedic physical therapists and hand rehabilitation
- Provide information for payers and claims reviewers regarding the practice of orthopaedic and hand therapy for common musculoskeletal conditions
- Create a reference publication for clinicians, academic instructors, clinical instructors, students, interns, residents, and fellows regarding the best current practice of orthopaedic physical therapy and hand rehabilitation

STATEMENT OF INTENT

These guidelines are not intended to be construed or to serve as a standard of medical care. Standards of care are determined on the basis of all clinical data available for an individual patient and are subject to change as scientific knowledge and technology advance and patterns of care evolve. These parameters of practice should be considered guidelines only. Adherence to them will not ensure a successful outcome in every patient, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgment regarding a particular clinical procedure or treatment plan must be made in light of the clinical data presented by the patient, the diagnostic and treatment options available, and the patient's values, expectations, and preferences. However, we suggest that significant departures from accepted guidelines should be documented in the patient's medical records at the time the relevant clinical decision is made.

Methods

The Academy of Hand and Upper Extremity Physical Therapy and the Academy of Orthopaedic Physical Therapy, APTA Inc. appointed content experts to develop clinical practice guidelines (CPGs) for musculoskeletal conditions of elbow, forearm, wrist, and hand. These content experts were given the task to identify impairments of body function and structure, activity limitations, and participation restrictions, described using ICF terminology, that could 1) categorize patients into mutually exclusive impairment patterns upon which to base intervention strategies, and 2) serve as measures of changes in function over the course of an episode of care. The second task given to the content experts was to describe the supporting evidence for the identified impairment pattern classification as well as interventions for patients with activity limitations and impairments of body function and structure consistent with the identified impairment pattern classification. It was also acknowledged by the Academy of Orthopaedic Physical Therapy, APTA content experts that only performing a systematic search and review of the evidence related to diagnostic categories based on International Statistical Classification of Diseases and Health Related Problems (ICD)[298] terminology would not be sufficient for these ICF-based CPGs as most of the evidence associated with changes in levels of impairment or function in homogeneous populations is not readily searchable using the ICD terminology. Thus, the authors of this guideline independently performed a systematic search of the MEDLINE, CINAHL, and the Cochrane Database of Systematic Reviews (1967 through November 2018) for any relevant articles related to classification, examination, and intervention strategies for carpal tunnel syndrome (CTS). Additionally, when relevant articles were identified their reference lists were hand-searched in an attempt to identify other relevant articles. Articles from the searches were compiled and reviewed for accuracy by the authors. [See **APPENDIX A** for full search strategies and **APPENDIX B** for search dates and results]

The authors declared relationships and developed a conflict management plan which included submitting a Conflict of Interest form to the Academy of Orthopaedic Physical Therapy, APTA, Inc. Articles that were authored by a reviewer were assigned to an alternate reviewer. Funding was provided by the APTA to the CPG development team for travel and expenses to the CPG development workshop. The CPG development team maintained editorial independence.

Articles contributing to recommendations were reviewed based on specified inclusion and exclusion criteria with the goal of identifying evidence relevant to physical therapist clinical decision-making for adults with Carpal Tunnel Syndrome. The title and abstract of each article were reviewed independently by 2 members of the CPG development team for inclusion. [See **APPENDIX C** for Inclusion and Exclusion criteria, available at www.jospt.org]. Full text review was then similarly conducted to obtain the final set of articles for contribution to recommendations. Additional CPG team members (MLE and CKC) provided the final decision for discrepancies that were not resolved by the review team. [See **APPENDIX D** for flow chart of articles and **APPENDIX E** for articles included in recommendations by topic, available at www.jospt.org]. For selected relevant topics that were not appropriate for the development of recommendations, such as incidence and imaging, articles were not subject to systematic review process and were not included in the flow chart. Evidence tables for this CPG are available on the Clinical Practice Guidelines page of the Academy of Orthopaedic Physical Therapy of the APTA website: www.orthopt.org.

This guideline was issued in 2019 based upon publications in the scientific literature prior to November 2018. This guideline will be considered for review in 2023, or sooner if clinically significant new evidence becomes available. Surveillance will include monitoring MEDLINE and CINAHL additions using feeds related to the search terms. Any updates to the guideline in the interim period will be noted on the Academy of Orthopaedic Physical Therapy of the APTA website: www.orthopt.org.

LEVELS OF EVIDENCE

Individual clinical research articles were graded according to criteria adapted from the Centre for Evidence-Based Medicine, Oxford, United Kingdom (http://www.cebm.net) for diagnostic, prospective, and therapeutic studies.[227] If the 2 content experts did not agree on a grade of evidence for a particular article, a third content expert was used to resolve the issue. [See **APPENDIX F** and **G** for Levels of Evidence table and details on procedures used for assigning levels of evidence, available at www.orthopt.org]. The evidence update was organized from highest level of evidence to lowest level. An abbreviated version of the grading system is provided below.

I	Evidence obtained from systematic reviews, high quality diagnostic studies, prospective studies, or randomized controlled trials
II	Evidence obtained from lesser-quality diagnostic studies, systematic reviews, prospective studies, or, randomized controlled trials (eg, weaker diagnostic criteria and reference standards, improper randomization, no blinding, <80% follow-up)
III	Case controlled studies or retrospective studies
IV	Case series
V	Expert opinion

STRENGTH OF EVIDENCE AND GRADES OF RECOMMENDATIONS

The overall strength of the evidence supporting recommendations made in these guideline were graded according to guidelines described by Guyatt et al,[122] as modified by MacDermid et al[173] adopted by the coordinator and reviewers of this project. In this modified system, the typical A, B, C, and D grades of evidence have been modified to include the role of consensus expert opinion and basic science research to demonstrate biological or biomechanical plausibility.

The strength of the evidence supporting the recommendations was graded according to the information provided below. Each team developed recommendations based on the strength of evidence, including how directly the studies addressed the question on hand pain and sensory deficits: carpal tunnel syndrome. In developing their recommendations, the authors considered the strengths and limitations of the body of evidence and the health benefits, side effects, and risks of tests and interventions

GRADES OF RECOMMENDATION		**STRENGTH OF EVIDENCE**
A	Strong Evidence	A preponderance of level I and/or level II studies support the recommendation. This must include at least 1 level I study
B	Moderate Evidence	A single high-quality randomized controlled trial or a preponderance of level II studies support the recommendation
C	Weak Evidence	A single level II study or a preponderance of level III and IV studies, including statements of consensus by content experts, support the recommendation
D	Conflicting Evidence	Higher-quality studies conducted on this topic disagree with respect to their conclusions. The recommendation is based on these conflicting studies
E	Theoretical/ Foundational Evidence	A preponderance of evidence from animal or cadaver studies, from conceptual models/principles, or from basic sciences/bench research support this conclusion
F	Expert Opinion	Best practice based on the clinical experience of the guidelines development team

GUIDELINE REVIEW PROCESS AND VALIDATION

Identified reviewers who are experts in management and rehabilitation reviewed this CPG content and methods for integrity, accuracy, and that it fully represents the condition. Any comments, suggestions, or feedback from the expert reviewers were delivered to the author and editors to consider and make appropriate revisions. These guidelines were also posted for public comment and review on the orthopt.org web site and a notification of this posting was sent to the members of the Academy of Orthopaedic Physical Therapy, APTA, Inc. Any comments, suggestions, and feedback gathered from public commentary were sent to the authors and editors to consider and make appropriate revisions in the guideline. In addition, a panel of consumer/patient representatives and external stakeholders, such as claims reviewers, medical coding experts, academic educators, clinical educators, physician specialists, and researchers also reviewed the guideline and provided feedback and recommendations that were given to the authors and editors for further consideration and revisions. Lastly, a panel of consumer/patient representatives and external stakeholders and a panel of experts in physical therapy practice guideline methodology annually review the Academy of Orthopaedic Physical Therapy, APTA's ICF-based Clinical Practice Guideline Policies and provide feedback and comments to the

Clinical Practice Guideline Coordinator and Editors to improve the Association's guideline development and implementation processes.

DISSEMINATION AND IMPLEMENTATION TOOLS

In addition to publishing these guidelines in the Journal of Orthopaedic & Sports Physical Therapy (JOSPT), these guidelines will be posted on CPG areas of both the JOSPT and the Academy of Orthopaedic Physical Therapy, APTA websites, and will be submitted for posting on ECRI Guidelines Trust (https://guidelines.ecri.org). The implementation tools planned to be available for patients, clinicians, educators, payors, policy makers, and researchers, and the associated implementation strategies are listed in **TABLE 1**:

TABLE 1: Planned strategies and tools to support the dissemination and implementation of this clinical practice guideline

Tool	Strategy
"Perspectives for Patients" and/or "Perspectives for Practice"	Patient-oriented guideline summary available on jospt.org and orthopt.org
Mobile app of guideline based exercises for patient/clients and healthcare practitioners	Marketing and distribution of app using www.orthopt.org
Clinician's Quick-Reference Guide	Summary or guideline recommendations available on www.orthopt.org
Read-for-credit continuing education units	Continuing Education Units available for physical therapists and athletic trainers
Webinars educational offering for healthcare practitioners	Guideline-based instruction available for practitioners on www.orthopt.org
Mobile and web-based app of guideline for training of healthcare practitioners	Marketing and distribution of app using www.orthopt.org
Physical Therapy National Outcomes Data Registry	Support the ongoing usage of data registry for common musculoskeletal conditions (www.ptoutcomes.com)
Logical Observation Identifiers Names and Codes mapping	Publication of minimal data sets and their corresponding Logical Observation Identifiers Names and Codes for the knee region on www.orthopt.org
Non-English versions of the guidelines and guideline implementation tools	Development and distribution of translated guidelines and tools to JOSPT's international partners and global audience

CLASSIFICATION

The primary International Classification of Diseases 10th Revision (ICD-10), and ICF codes for CTS are provided below:

Category	Descriptor	Code
ICD-10CM		
	Carpal tunnel syndrome unspecified upper limb	**G56.00**
	Carpal tunnel syndrome right upper limb	**G56.01**
	Carpal tunnel syndrome left upper limb	**G56.02**
	Pain in the right hand	**M79/641**
	Pain in the left hand	**M79.642**

	Pain in unspecified hand	**M79.643**
	Pain in right fingers	**M79.644**
	Pain in left fingers	**M79.645**
	Pain in unspecified fingers	**M79.646**
	Hypoesthesia of skin	**R 20.1**
	Paresthesia of skin	**R 20.2**
	Unspecified disturbances of skin sensation (includes temperature, localization, tactile discrimination, texture, vibration.	**R 20.9**
ICF body structure code		
	Structure of the nervous system other specified	**s198**
	Structure of hand	**s7302**
	Muscles of the hand	**s73022**
ICF body function codes		
	Sleep functions	**b134**
	Maintenance of sleep cycle	**b1342**
	Proprioceptive function	**b260**
	Touch function	**b265**
	Sensory functions related to temperature and other stimuli	**b270**
	Sensitivity to vibration	**b2701**
	Sensitivity to pressure	**b2702**
	Sensation of pain	**b280**
	Radiating pain in a segment or region	**b2804**
	Pain in upper limb	**b28014**
	Power of isolated muscles and muscle groups	**b7300**
	Control of simple voluntary movements	**b7600**
	Coordination of voluntary movements	**b7602**
	Protective functions of the skin	**b810**
ICF activities and participation codes		
	Writing	**d170**
	Carrying out daily routine	**d230**
	Using telecommunication devices and techniques	**d3600**
	Fine hand use	**d440**
	Picking up	**d4400**
	Grasping	**d4401**
	Manipulating	**d4402**
	Fine hand use other specified	**d4408**
	Driving	**d475**
	Toileting	**d530**
	Dressing	**d540**
	Eating	**d550**
	Drinking	**d560**
	Preparing meals	**d630**
	Doing housework	**d640**
	Remunerative employment	**d850**

SCOPE AND ORGANIZATION OF THE GUIDELINE

This guideline includes information related to incidence, prevalence, anatomy, pathoanatomy, clinical course, risk factors, diagnosis, outcomes assessment, and interventions for CTS. Where

appropriate, sections contain a summary or evidence synthesis and a statement describing gaps in knowledge. Grades of recommendation have been provided for areas related to clinical practice including diagnosis, outcomes assessment, and interventions. The use of and recommendations for specific diagnostic tests such as nerve conduction studies, electromyography, magnetic resonance imaging, and ultrasonography are beyond the scope of this guideline and could serve as future CPG topics.

PREVALENCE AND INCIDENCE

I

The overall lifetime prevalence of CTS in the general population is 8.0%.[165] Prevalence, when confirmed by both electrodiagnostic testing and clinical examination is 7.8% in the U.S. working population.[77] For women, the prevalence is nearly twice that for men (10% compared to 5.8%). There is a marked increase in prevalence with increasing age, 3.7% in those younger than 30 compared to 11.9% in those over 50 years of age.[51]

Incidence data, reported as part of the Rochester Epidemiology Project, dating from 1981 to 2005 show the incidence in the general population is 3.76 per 1000 person-years (4.91 for women and 2.58 for men).[106] Incidence data collected from France show a lower incidence rate (1.4/1000 person-years in women and 0.6/1000 person-years in men).[249]

When comparing data from 1981 to 1985 to data from 2001 to 2005, the incidence of CTS increased from 2.58 per 1000 person-years to 4.24 per 1000 person-years.[106] Data from 2007 to 2011 also show an increase in occupational-related CTS.[248] The increase may be due to greater awareness and more patients presenting for care.[106]

Incidence rates derived from the working population are reportedly higher than those for the general population.[77, 249] The overall incidence in this group is 23 per 1000 person years when CTS was confirmed through both clinical exam and electrodiagnostic studies.[77] When the diagnosis was confirmed by symptoms alone, the incidence was much higher (93 per 1000 person years). When electrodiagnostic tests alone were used to confirm the diagnosis, the incidence was 40 per 1000 person years.[77]

ANATOMICAL AND PATHOANATOMICAL FEATURES

Anatomical features

The carpal tunnel is formed by the carpal bones and the transverse carpal ligament. The tunnel circumference is rigid with bony dorsal boundaries and the stiff palmar boundary formed by the transverse carpal ligament. The ligament spans from the pisiform bone and hook of hamate on the ulnar side to the scaphoid and trapezium tubercles on the radial side. Nine flexor tendons pass through the carpal tunnel: 4 tendons from the flexor digitorum superficialis (FDS) muscle, 4 from the flexor digitorum profundus (FDP) muscle, and a single tendon from the flexor pollicis longus (FPL) muscle. The tendons of the FDS and FDP are arranged in 2 rows, with the FDS tendons more palmar and the FDP tendons deeper, dorsal to the FDS tendons. The carpal tunnel contains 2 bursae, the radial bursa, which encases the FPL, and the ulnar bursa which surrounds the tendons of the FDS and FDP.[91] The median nerve is vulnerable to compression from external or internal forces because it is the most superficial structure in the carpal tunnel, lying between the transverse carpal ligament and the ulnar bursa.

Classic sensory and motor innervation of the median nerve in the hand (affected in patients with CTS) includes the sensory branches of the thumb, index, middle, and radial half of the ring

fingers, while the motor branches innervate the first and second lumbrical muscles, opponens pollicis, abductor pollicis brevis (APB), and the superficial portion of the flexor pollicis brevis muscles. The sensation to the skin directly over the carpal tunnel and the thenar eminence is typically not affected, because these areas are supplied by the palmar cutaneous branch which branches off the median nerve approximately 5 cm proximal to the wrist crease.[149] The area over the scaphoid tubercle is also spared in CTS because its innervation comes from the lower antebrachial cutaneous nerve.

Mackinnon[175] described the blood supply to the median nerve as being from the radial and ulnar arteries and running to the nerve from the superficial palmar arch. The vessels coil the nerve which ensures an adequate blood supply during nerve gliding. Blood flows from these vessels into the vasoneurium and then into the epineurial space. Vessels run in a plexus formation in the epineurium and perineurium, reaching the endoneurium as only a fine network of capillaries.[175] Changes in the blood supply have been implicated in the development of CTS and is described below.

Pathoanatomical features

Classic CTS symptoms are numbness and tingling in the median nerve distribution of the hand, and in more severe cases, loss of strength of muscles innervated distally by the median nerve. Median nerve pathology impacts all nerve functions distal to the site of lesion with some possible pain being felt proximally to the shoulder. Even though the definition seems straightforward, controversy abounds regarding its etiology. A variety of pathoanatomical factors have been implicated in the development of CTS including elevated carpal tunnel pressure, ischemic changes within the nerve, and compression from adjacent structures.

Elevated carpal tunnel pressure

II

Chen et al[62] studied the validity of carpal tunnel pressure as a source for median nerve compression. Tunnel pressure was measured at various points in patients undergoing carpal tunnel release (CTR) surgery. The highest mean (+/- standard deviation) tunnel pressure before surgery was 58.9 +/- 3.4 mmHg and following surgery was 7.7 +/- 0.9 mmHg, confirming pre-operative elevated tunnel pressure and confirming the usefulness of CTR surgery to lower pressure.

Chen et al[62] reported an association between elevated tunnel pressure and loss of median nerve function as measured by moderate correlations between tunnel pressure and findings from nerve conduction studies (NCS) (r=0.53 for distal motor latency [DML], r=0.47 for sensory nerve action potential [SNAP], r=-0.54 for sensory nerve conduction velocity [SNCV], and r=-0.27 for compound muscle action potential [CMAP]). However, pre-operative pressure was not related to 3-month post-operative outcomes as measured by the Boston Carpal Tunnel Questionnaire Symptom Severity Scale (CTQ-SSS). Instead, Chen et al[62] concluded that NCS results better predicted 3-month outcome.

III

Ahn et al[2] evaluated carpal tunnel pressures in patients with CTS and recorded structural findings from ultrasound (US) imaging and nerve conduction measures. Elevated pressure was confirmed pre-operatively with the mean tunnel pressure being 56.7 mmHg distal to the incision site and 18.2 mmHg proximal to the incision site. After CTR surgery, pressure decreased to 7.4 mmHg distally and 7.5 mmHg proximally (P< .05).

Ahn et al[2] reported maximum tunnel pressure was not different between patients with moderate, severe, or extreme pathology classified based on the NCS results, even though median nerve cross sectional area differed between individuals with different NCS-severities. Ahn et al[2] suggested that intra neural pressure may be more relevant than tunnel pressure. Due to the conflicting findings between the aforementioned studies,[2, 62] Chen et al[62] concluded there may be another mechanism of median nerve damage besides those attributed to pressure.

V

Gelberman et al[104] compared carpal tunnel pressure between those with and without CTS. They reported a statistically significant higher carpal tunnel pressure in the patient group when compared to the controls with the wrist in a neutral position (P<.001), a flexed position (P<.005), and an extended position (P<.010). Wrist position affected pressure for patients and controls, with the lowest pressure in neutral and higher pressures in flexion and extension. Immediately following CTR surgery, pressure decreased in the patient group to 5.0 mmHg.

Ischemia and nerve fibrosis

V

In a narrative review of basic science literature including animal and human studies, Gelberman et al[105] described a gradual decrease in intraneural blood flow with experimental compression from 50 to 80 mmHg and complete ischemia at 80 mmHg. Findings from both animal and human studies show increased epineural edema and endoneurial fluid pressure related to the magnitude and duration of the compression.

V

In a subsequent narrative review, Mackinnon[175] described the mechanism between ischemia, neural edema, and fibrosis. She indicated that nerve compression leads to breakdown in the blood nerve barrier at the endoneurial vessels, causing a leakage of fluid into the endoneurium. If the barrier in the inner layers of the perineurium remains intact, the endoneurial fluid pressure will increase and result in a mini compartment syndrome within the fascicle. She described this breakdown and leakage of fluid as causes that lead to the accumulation of proteins, lymphocytes, fibroblasts, macrophages, and eventually scar formation, or nerve fibrosis.

Compression from adjacent structures

III

Freeland et al[101] studied the presence of prostaglandins (PGE_2) and interleukins (IL-1 and IL-6) in serum and the tenosynovium in those with CTS and a control group. These authors found

elevated IL-6 and PGE_2 levels in the tenosynovium in those with CTS compared to the control group. These chemicals have been associated with stimulating tissue fibrogenesis.[101] There was no significant difference in IL-1 levels between the 2 groups. This latter finding supports the lack of acute inflammation in the tendon sheath when assessed at the time of surgery.[101]

III

The subsynovial connective tissue (SSCT) is a highly vascular layer between the flexor tendons and ulnar bursa. Ettema et al[91] examined the histology and immunohistochemistry of the SSCT of individuals undergoing CTR surgery for idiopathic CTS. There was a marked increase in fibroblast density, collagen fiber size, vascular proliferation, and collagen-type III in the patient group compared to the control group. The presence of collagen-type III is important because it is inherently weak and could possibly predispose an individual to a cycle of further injury.[91] There was also a significantly greater amount of transforming growth factor-β in the patient group compared to the control group. Transforming growth factor-β is a profibrotic cytokine present during wound healing and plays a role in fibrosis and scarring. Authors of other Level 3 studies have identified similar changes in the tenosynovium in individuals with CTS.[132, 272]

Summary

Elevated carpal tunnel pressure has been implicated in the development of CTS and studies support elevated pressure in patients just prior to surgery that decrease post-operatively. The etiology behind the elevation in pressure is unknown. Bench research suggests there is a disruption in intraneural blood flow that contributes to intraneural edema and fibrosis. Enlargement of the flexor tendon synovial sheaths, such as in flexor tenosynovitis, has been implicated as the source contributing to median nerve compression. However, models suggesting acute inflammation within the sheath are not well-supported.[101, 200] Instead, there is evidence to support fibrous synovial hypertrophy in individuals undergoing surgical release for idiopathic CTS.[91, 101, 132, 272]

CLINICAL COURSE

II

In a systematic review, Burton et al[50] reported that some patients (28-62%) recover without intervention while others (32-58%) deteriorate in the absence of intervention. In patients who undergo non-surgical management, authors reported that 57% progress to surgery in 6 months, 58% progress to surgery in 1 year, and 62-66% progress to surgery in 3 years.[50]

II

Three studies not included in the Burton systematic review reported outcomes following non-surgical management in patients with CTS who did not have thenar muscles atrophy.[27, 110, 230] Povlson et al[230] enrolled 75 patients, and at the end of 3 months, 52 (69%) were satisfied with their outcome while 17 (23%) progressed to surgery. Of the 52 who were satisfied at 3 months, 30 responded to a follow-up questionnaire presented 33 months after concluding the original treatment. Of the 30 (63% female) who responded, 13 were still satisfied with the wrist orthosis, 14 had undergone surgery, and 3 were not satisfied and were contemplating surgery. Baker and Livengood[27] analyzed baseline, 3-month, and 6-month data from patients who had participated in

a randomized clinical trial (RCT) using a wrist orthosis. Their results indicated that 21 (22%) of 96 individuals who completed their study went on to have surgery. Gerritsen et al[110] reported a 12-month success rate of 31% for use of a neutral night wrist orthosis for 6 weeks.

II

Ollivere et al[213] found that 14 (16%) of 89 hands of 58 individuals with CTS (all severities) improved with non-surgical treatment alone, while 75 (84%) of the 89 hands underwent CTR surgery during or after 3 months of non-surgical management consisting of a steroid injection, night wrist orthosis, tendon gliding exercises, and simple analgesia.

II

Researchers have examined factors that predict progression to surgery. Burton et al[50] found that symptom duration, a positive Phalen test, and thenar eminence muscle wasting were associated with poor outcomes with non-surgical management. Gerritsen et al[110] reported that shorter symptom duration (<1 year) and lower severity of night-time symptoms (score of <6/10) were the best predictors of success with non-surgical management. Baker and Livengood[27] reported that having more than 1 non-surgical intervention was a predictor of progression to surgery (odds ratio [OR] 24.3; 95% CI 4.3, 138.2). Four studies examined the use of the CTQ-SSS[162] as a prognostic indicator for progression to surgery with conflicting results that will be discussed in the Outcome Measures section.[44, 110, 147, 213]

IV

Capasso et al[54] followed 24 individuals classified as having severe idiopathic CTS based on electrodiagnostic and clinical findings. Long-term outcomes for untreated patients (n=9) and those receiving non-surgical management (n=3) were poor. At the time of the re-evaluation, which ranged from 1 to 9 years after diagnosis, 90% of the patients continued to have pain and/or paresthesia, and all patients showed thenar eminence muscle atrophy, loss of strength ("plegia") of the APB, hyperesthesia, and absence of median nerve conduction responses. The 12 individuals who had CTR surgery showed signs of electrophysiological re-innervation and objective recovery in all but 1 case. When comparing groups, those who underwent CTR surgery showed better resolution of pain and paresthesia, lower CTQ scores, improvement in APB strength, and reappearance of CMAP and SNAP. Hyperesthesia remained unchanged in both groups.

Evidence Synthesis and Clinical Rationale

The likelihood of patient successful response to non-surgical management is unknown. There is evidence that some patients benefit from non-surgical management, and for some patients, non-surgical management is curative. There is conflicting evidence on the percentage of individuals who progress to surgery after failed non-surgical management ranging from 23%[230] to 84%[213] after 3 months and 57 to 58% at 6 months and 1 year, respectively.[50] There are some single studies that have identified factors that predict progression to surgery, but these need validated in larger studies. More research is needed to identify the characteristics of patients who benefit from non-surgical management versus those who can achieve positive outcomes only through surgical management. In light of a preponderance of studies reporting fairly high rates of

progression to surgery, clinicians must measure progress carefully and refer patients for surgical consultation if improvement with non-surgical management is not observed.

Summary
Clinicians should assess symptom duration, severity of nighttime symptoms, presence of a positive Phalen test, presence of thenar eminence muscle wasting, and prior non-surgical interventions for an individual with CTS and adjust the prognosis accordingly.

CLASSIFICATION

Carpal tunnel syndrome can be acute or chronic. Acute CTS is relatively rare and has various causes such as: spontaneous bleeding, thrombosis, dislocation of a metacarpal base, infection, pregnancy, and fractures, with distal radius fractures being the leading cause.[105] Chronic CTS has a gradual onset, sometimes presenting in an individual finger and later spreading to the remaining median nerve distribution.[271] The initial onset of symptoms is usually at night, but as symptoms worsen, individuals may complain of symptoms throughout the day along with clumsiness and difficulty with grip and pinch.[271]

Carpal tunnel syndrome is most commonly classified by severity, i.e., mild, moderate, severe, or extreme. Classification systems reported in the literature are largely based on data from electrophysiological studies.[39, 49, 57, 118, 137, 221, 287] Rempel et al[239] provided consensus criteria for classifying CTS in epidemiologic studies, however, these criteria were not intended for clinical diagnosis or management.

III

In a recent study, Roll et al[247] reported on an 8-point scoring system that combined clinical criteria (Phalen test, Tinel sign, Durkan test, the Boston Carpal Tunnel Questionnaire Symptom and Functional Scales) with ultrasound findings to determine severity of CTS. Authors concluded the system accurately classified 79.8% of participants into the correct severity based on electrodiagnostic studies.

III

Caliandro et al[52] examined severity based on the patient's distribution of symptoms. They found that the likelihood of having a median-distribution presentation increased with increasing severity (OR=2.07, 95% CI 1.51, 2.83) as measured on NCS. Also, patients with mild and moderate severity CTS were more likely to present with a stocking-glove paresthesia distribution.

V

There were 2 classification systems published by Gelberman et al[105] and Szabo and Madison,[271] similarly based on a combination of clinical and electrodiagnostic findings. According to Gelberman et al,[105] mild CTS included: symptom duration less than 1 year; diffuse complaints; intermittent numbness; normal 2-point discrimination (2PD); and absence of weakness or atrophy. Nerve conduction velocities were increased only by 1 to 2 ms, and there were no

fibrillations on electromyographic testing. Intermediate CTS included constant paresthesia and numbness, elevated threshold values, and increased DMLs. Advanced CTS was characterized by permanent sensory and motor loss and thenar muscle atrophy. The classification outlined by Szabo and Madison[271] was similar in terms of electrodiagnostic findings. In early CTS, sensory latencies are more likely to be prolonged than motor latencies; intermediate CTS included constant sensory deficits and possible motor impairment; and advanced CTS included severe loss of sensory and motor function as well as thenar muscle atrophy.

V

Maggard et al[178] also outlined a severity scale based on a literature review. In their classification, mild disease included all 3 of the following: 1) symptom pattern at least characteristic of CTS; 2) intermittent symptoms; and 3) no abnormalities of physical exam. Moderate CTS included: 1) symptom pattern at least characteristic of CTS; 2) no thenar atrophy; and 3) at least 1 of the following: constant symptoms, thenar musculature weakness, or loss of sensory function in fingers I, II, or III. Severe disease included: 1) symptom pattern at least characteristic of CTS; and 2) thenar muscle atrophy. In a Delphi consensus study, Graham et al[117] indicated that thenar muscle atrophy, location/presence of sensory symptoms, nocturnal symptoms, and APB weakness were among the top 5 diagnostic criteria identified by participating physicians.

V

Mackinnon[175] provided a classification based on the Sunderland stages of nerve injury that included pathophysiological changes and electrodiagnostic findings. It was later expanded upon by MacDermid and Doherty[170] to include clinical exam findings based on pathophysiology. In a grade 1 injury (neuropraxia), there is conduction block, and there may be some areas of segmental demyelination. The axon is uninjured and does not need to undergo regeneration. Provocative testing that increases pressure on the nerve is likely to result in increased paresthesia. Sensory changes should be evident in the largest nerve fibers and thus the patient would have diminished touch and vibration threshold. A grade 2 injury (axonotmesis) involves axonal injury and may show signs of remyelination, therefore one may suspect a positive Tinel sign and 2PD changes. Patients may no longer experience paresthesia but numbness instead, and there may be a noticeable loss of strength. A grade 3 injury has axonal loss and scarring in the endoneurium, and patients have constant numbness and observable thenar muscles atrophy.[170, 175]

Summary

There is a lack of consensus on clinical classification of CTS, especially in the absence of electrodiagnostic studies. Classifications based on clinical signs and symptoms alone or combined with electrodiagnostic studies are largely based on anecdotal evidence, expert consensus, or the pathophysiology of nerve compression and lack independent validation. According to evidence presented, the frequency of symptoms (mild demonstrating more intermittent symptoms and moderate demonstrating more constant symptoms) seems to be a factor that distinguishes mild from moderate CTS, and thenar muscles atrophy is the clinical sign that distinguishes patients with severe CTS from those with mild or moderate disease.

DIFFERENTIAL DIAGNOSIS

The most common differential diagnoses include cervical radiculopathy, thoracic outlet syndrome, diabetic neuropathy and pronator teres syndrome. Others include ulnar and radial

tunnel syndrome. Differentiating between CTS and other conditions, musculoskeletal and non-musculoskeletal is outside the scope of this review.

RISK FACTORS

Intrinsic Risk Factors

Obesity

Several authors suggest that obesity increases fatty tissue and/or hydrostatic pressure within the carpal tunnel producing compression on the median nerve. Others theorize that metabolic changes occur in obesity causing endoneurial edema and intrafascicular swelling of the median nerve.[261, 304] Obesity is one component of metabolic syndrome which has been associated with dative stress.[261]

I

In a study of 3515 participants followed prospectively for up to 7 years, the risk of developing CTS in the right dominant hand was noted to increase linearly as body mass index (BMI) rose.[127] Having a BMI $\geq$30 kg/m^2 nearly doubled the risk of developing CTS (Hazard ratio (HR)= 1.67; 95% CI 1.26 to 2.21).

II

The majority of prospective studies[18, 36, 40, 74] and 1 meta-analysis[261] demonstrated that the risk of developing CTS increases linearly with increasing BMI and the risk at least doubles for those individuals with a BMI >30 kg/m^2. The sole study that did not find an association suggested the reason for this was the low power in the study (109 individuals with obesity in a sample of 1611 workers).[226] Additionally, BMI was strongly and positively correlated with slowing of median nerve conduction found in a 5-year follow-up of industrial workers.[36]

III

A significant number of additional studies support obesity as a risk factor for CTS[40, 66, 74, 75, 81, 85, 93, 133, 140, 152, 158, 187, 194, 196, 198, 202, 245, 273] and higher BMI has been associated with increased risk for more severe forms of CTS.[75] The ability to diagnose CTS using BMI and other measures used to quantify abdominal adiposity (which have been shown to be better predictors of cardiovascular and other diseases) was assessed by Mondelli et al.[196] Although a high BMI, waist-hip-height ratio (waist circumference/hip circumference divided by height $\geq$ 0.53 for women and $\geq$ 0.54 for men) and waist-stature ratio (waist circumference/individual's height $\geq$0.54 for women and $\geq$ 0.57 for men) did predict those with severe CTS with sensitivity ranging from 72 to 92% (values varied by sex and whether compared to electrodiagnosis or clinical diagnosis); specificity did not reach levels for acceptable diagnostic accuracy (57 to 66%).

Age and Female Sex

The physiologic changes associated with aging have been suggested to predispose individuals to CTS, specifically vascular abnormalities and age-associated decreased axon number and

conduction velocity.[18] The reason for a potential higher incidence of CTS in the female sex is less clear. A hormonal mechanism is often proposed, as well as, women having a smaller cross-sectional area of the carpal tunnel compared to males.[81, 270] Other hypotheses include: more common reporting of symptoms; lower strength which produces a greater percentage of maximum voluntary contraction to complete the same tasks; and smaller stature leading to greater wrist deviations required at work stations.

I/II

Results from level I[127] and II studies[206, 249, 283] concur that increasing age and the female sex are risk factors for CTS. Specifically, the risk for CTS appears to increase linearly with age and more than doubles in those over the age of 50. Female sex increases the risk between 1.5 and 4 times compared to male counterparts.

III

Additional level III studies were located supporting increasing age[21, 36, 40, 75, 89, 93, 130, 152, 158, 187, 198, 202, 205, 243, 245, 270, 273, 290] and female sex as risk factors.[21, 36, 89, 93, 158, 187, 198, 266, 273, 290]

Diabetes Mellitus

Diabetes mellitus (DM) has been proposed to be associated with CTS. The mechanism by which this syndrome may influence the development of CTS is not completely understood. DM is known to cause peripheral neuropathy by glycosylation of protein end products that increase circulating inflammatory cytokines and vascular endothelial growth factor. These mediators may sensitize the median nerve to alterations within the carpal tunnel.[229, 266, 279] Oktayoglu et al[212] hypothesize that the increased osmotic pressure arising from intracellular sorbitol accumulation in diabetes may result in edema and hydropic degeneration. DM may also produce vascular changes and tendinopathy leading to CTS.[266] In fact, Taser et al[274] have found an increased number of fibroblasts, collagen fiber diameter and lengths, as well as, neovascularization in the SSCT of patients with DM undergoing CTR surgery compared to those with idiopathic CTS or patients with hypothyroidism.

I

Harris-Adamson et al,[127] did not find DM to be a significant independent predictor for the development of CTS when the data was adjusted for sex, age, and BMI.

II

A random effects meta-analysis[229] and a large prospective study,[61] however, both found significantly higher risk of CTS in those with DM. The risk was similar whether the individual had Type 1 or 2 diabetes.[229]

III

Authors of 6 studies[36, 120, 130, 198, 212, 279] found significant associations and 1 found no association between DM and CTS.[89] Those reporting an OR found increased risk of CTS in the presence of

DM to be in the range of 1.24 to 2.2. Oktayoglu et al[212] demonstrated that patients with type 2 diabetes had significantly higher incidence of CTS than even individuals with hypothyroidism or acromegaly. In the one study, where authors found no association between CTS and DM, the relative risk was 1.26 (95% CI:0.65–2.44), and it did not reach statistical significance.[89]

Rheumatoid Arthritis (RA)

Synovial expansion, joint erosion, and ligament laxity that occurs with RA may result in loss of carpal tunnel height and increased pressure on the median nerve.[251]

I

RA was not found to be a significant, independent predictor for the development of CTS when the data were adjusted for sex, age, and BMI in a study by Harris-Adamson et al.[127]

II

In contrast, even when adjusting for age and sex, Shiri's[256] meta-analysis of studies that examined the risk of CTS in individuals with RA found and increased risk with a pooled OR of 1.96 (95% CI 1.57-2.44, I2 =32.2%).

III

Two systematic reviews provided conflicting findings,[251, 279] and 1 primary study[89] found no association between RA and CTS. Specifically, the pooled data from 8 studies in Sakthiswary and Singhb's[251] meta-analysis revealed that 5.5% patients with RA had CTS which is similar to the prevalence of CTS in the general population (2.7 to 5.8%).

Cardiovascular risk factors

III

Hypercholesterolemia has been associated with upregulating growth factors responsible for fibrogenesis in various organs and peripheral nerves. Nakamichi and Tuchibana[201] hypothesize that this may increase connective tissue within the median nerve leading to increased risk of CTS. These authors found that the prevalence of CTS and median nerve cross sectional area within the carpal tunnel increased significantly as low density lipoproteins (LDL) levels increased. Although obesity was more prevalent in the CTS group, obesity was not found to be a significant factor in the logistic regression model.

III

Shiri et al[260] found cardiovascular risk factors to be associated with CTS in a large cross-sectional study. The specific risk factors varied based on age. In the younger age group (30-44 years), the following risk factors were associated with CTS: obesity, high LDL cholesterol, high triglycerides, hypertension, and cardiac arrhythmia. In the older age group (> 60 years),

coronary artery disease, valvular heart disease, and carotid artery intima-media thickness were associated with higher risks of CTS. Hegmann et al[130] found an association between CTS and the cardiovascular disease risk factor score which included: age, hypertension, tobacco use, and DM.

Osteoarthritis and Previous Musculoskeletal Disorders

One theory for how osteoarthritis may predispose to CTS is that hypertrophy of carpal bones narrows the tunnel and thereby produces compression of the median nerve. The reason for previous musculoskeletal disorders leading to CTS is less clear. Werner et al[291] suggests 1) that individuals with pain in other parts of the upper extremity may develop compensatory strategies that place higher loads and awkward positioning of the hand and wrist or 2) because CTS can refer pain to the elbow or shoulder, patients with CTS may be misdiagnosed as having various tendinopathies. Ferry et al[97] also propose that mechanical problems in the cervical area may contribute to multiple disorders of the upper limbs.

II

Individuals with a history of wrist or hand tendinopathies had increased odds of developing CTS in a prospective study of employees in an automotive assembly plant (OR = 4.74; 95% CI 1.09, 20.43).[289] In Shiri's[256] meta-analysis of individuals with OA, 2 studies consisting of 19 480 participants were pooled and data were adjusted for age and sex. The OR for development of CTS was 1.87 (95% CI 1.64, 2.13, I2=0%) in individuals with OA.

III

Level III studies have found an association between CTS and the following musculoskeletal disorders: 1) prior distal upper extremity disorders (OR=3.48, 95% CI 2.56, 4.73)[93]; 2) arm fracture, OA of the spine, tennis elbow, and joint pain (OR=1.98, 95% CI 1.61-2.42)[97]; 3) lupus, disc disease, OA, or RA (OR=2.4 95% CI 1.24, 4.67)[209]; 4) cervical spine complaints or previous upper limb trauma (OR= 4.57 95% CI 2.28, 9.14 and 8.09 95% CI 2.35, 27.91, respectively)[243]; and 5) rotator cuff syndrome (OR =1.84, CI not reported).[56]

Hypothyroidism

Several mechanisms on how hypothyroidism may contribute to the development of CTS have been proposed including: synovial thickening surrounding flexor tendons, deposition of pseudomucinous material on the median nerve, alterations in fluid balance, and increased peripheral edema.[143, 212, 257, 274]

III

Two meta-analysis have been performed which assessed the association between hypothyroidism and CTS. Shiri,[257] when including only the 4 studies that controlled for potential confounders, found a significant association (effect size (ES)=1.44; 95% CI 1.27, 1.63, I2 50%). Van Dijk et al[279] found a pooled OR of 1.4 (95% CI 1.0, 2.0) in their analysis of 9 articles. Two of 3 other studies[157, 198, 212, 244] not included in the above meta-analyses, concurred that hypothyroidism is a risk factor for CTS.

Genetic Predisposition

III

Hemminki et al[131] compared hospitalized sibling pairs affected with a nerve, nerve root, or plexus disorder to hospitalized sibling pairs without any neurological disorders. The calculated sibling risk for a neurological disorder when one sibling had CTS was 4.08. Sibling risk for CTS when one sibling had CTS increased to 6.18 (95% CI 2.88, 12.73). In a multicenter population-based case-control study, Mattioli et al[186] found that the odds of CTS development increased 7 fold in those whose sibling had a history of CTS (OR=8.1 95% CI 2.3, 29.2). Whereas, Nordstrom et al[209] found twice the odds for development of the syndrome (OR=2.09 95% CI 1.28, 3.4) in individuals with a parent, sibling, or child with history of CTS. Bland[40] found that those with a family history of CTS were at increased odds for development of CTS only when under the age of 63 (OR=1.42 95% CI 1.14, 1.77). In a twin study, Hakim et al[124] calculated the case-wise concordance (the probability that a twin is affected, given that the co-twin is affected) was 0.35 in monozygotic twins compared to 0.24 in dizygotic. There was a significantly increased monozygotic to dizygotic ratio of 1.48 with an estimated genetic inheritance of 46%. When adjusting for other potential confounders, no other risk factor was significant. Radecki[234] noted significantly more individuals with CTS (27.3 %) also had positive family history compared to only 13.3% of those without confirmed CTS. A positive family history was predictive (chi-square = 20.48) of positive NCS with a relative risk of 1.35.

Wrist/Hand Anthropometrics

It has been proposed that individuals with a square-shaped wrist (versus rectangular) and those with shorter fingers or palm may be at increased risk for CTS because of a greater need for flexion and extension range of motion, and therefore, more force required to perform tasks.[18, 140] Over time this may increase carpal tunnel pressure.

Commonly measured, typically using a sliding digital caliper, wrist and hand anthropometrics, include: 1) wrist width--maximum distance at the level of the distal flexor wrist crease; 2) wrist depth--anteroposterior depth at the level of the distal flexor wrist crease; 3) palm length--distance between the distal flexor crease of the wrist to the proximal crease of the middle finger; 4) middle finger length--distance of the proximal flexor crease of the middle finger to the tip of the same finger); 5) hand length--distance between the distal flexor crease of the wrist to the tip of the middle finger; and 6) palm width--maximum distance between the heads of the second and fifth metacarpals. Commonly calculated indices include: 1) wrist ratio = wrist depth divided by wrist width; 2) wrist-palm ratio = wrist depth divided by palm length; 3) hand ratio = hand length divided by palm width; and 4) shape index = palm width x 100 divided by hand length.

Wrist Ratio (Square Wrist)

II

In the study by Nathan et al,[204] a higher wrist ratio (more square wrist) was the third most predictive factor (after BMI and increasing age) for maximum latency difference in sensory nerve conduction.

III

Shiri[258] completed a meta-analysis of 16 papers that studied the association between CTS and wrist ratio. The mean wrist ratio was higher in individuals with CTS compared with those without CTS (pooled mean difference [MD]=0.036). A more square-shaped wrist was associated with CTS with a pooled OR of 4.56 (95% CI 2.97, 6.99) and for those with a wrist ratio >0.70 the OR was 2.73 (95% CI 1.49, 5.01). This trend was true for both men and women. One of the studies in this review, Hlebs et al,[133] found the sensitivity and specificity using the >0.70 wrist ratio in determining those with and without CTS to be excellent (90% and 82%, respectively). In a more recent study, authors reported that a wrist ratio greater than .69 increased the odds of having CTS (OR 8.2 95% CI 1.2, 53.2).[216]

III

Authors of 3 other studies (not reviewed in Shiri's meta-analysis) found that a higher wrist ratio increases an individual's risk for CTS.[75, 194, 234] The mean $\pm$ standard deviation wrist ratio from these studies ranged from 0.68$\pm$0.04 to 0.75$\pm$0.05 for patients with CTS and 0.65$\pm$0.04 to 0.69$\pm$0.02 for those without. The cut-off value for the wrist ratio was set at $\geq$0.70 in the former 2 studies. Keeping the same cut off value for men but setting the cut-off value for women at >0.71, Mondelli et al[194] found the sensitivity ranged from 59% to 70% and specificity 48% to 59%. Positive and negative likelihood ratios were 1.35 to 1.44 and 0.62 to 0.69, respectively.

III

In a later study using the same subject population, Mondelli et al[196] noted that the wrist ratio was better at predicting those with severe CTS than CTS in general, especially for men. Values were calculated separately for men and women and clinical versus electrophysiologic diagnoses ranged from 69% to 79% for sensitivity, 48% to 59% for specificity, 1.32-1.76 for positive likelihood ratios (+LR) and 0.43 to 0.65 for negative likelihood ratios (-LR).

Hand Ratio/Shape index (short, wide hand)

III

Authors of 8 studies found that those with CTS had significantly shorter and wider hands than those without CTS. Three studies reported hand ratios,[66, 67, 140] 2 reported shape index,[45, 133] one assessed both values,[194] and 2 palm length/palm width.[18, 207] The mean $\pm$ standard deviation hand ratio ranged from 2.00$\pm$0.10 to 2.29$\pm$0.12 for CTS cases and 2.20$\pm$0.1 to 2.35$\pm$0.11 for controls. Shape index ranged from 44.85$\pm$3.19 to 46.8$\pm$2.4 for CTS cases and 42.31$\pm$2.7 to 45.0$\pm$2.1 for controls.

III

Of the 2 studies that calculated sensitivities and specificities,[194, 207] the best sensitivity (70.8%) was obtained for using the cut off value of <1.17 in palm length/width measure. The best specificity (71.1%) was found in using > 46.1 for shape index and <2.17 for hand ratio in men.

Wrist-palm ratio

III

Mondelli et al[194-196] found that the wrist-palm ratio was one of the best anthropometric indexes for predicting those at risk for CTS development. When controlling for age and sex, the relative risk ratio was 1.52 for mild, 1.85 for moderate, and 2.39 for severe CTS. The wrist-palm ratio was better than the wrist ratio in its diagnostic characteristics. With a cut off value of ≥0.39 for women and ≥0.40 for men; values obtained for identifying those with severe CTS ranged between 81-96% for sensitivity, 59-75% for specificity, 2.09-3.85 for +LR, and 0.06-0.25 for -LR. Identification of other severity levels of CTS was not as successful. Results were generally better for men than women and using clinical diagnosis versus electrophysiological data. The authors concluded that the wrist-palm ratio could be used to support a diagnosis of severe CTS.

III

Kouyoumdjian et al[155] found a significant progressive correlation between the wrist-palm ratio and severity of CTS ($P < .001$) for those with moderate to severe CTS. Wrist-palm ratios in these patients ranged from 0.38 to 0.40. No correlation was found between wrist-palm ratio and mild CTS.

Height

III

Six studies[66, 82, 85, 186, 194, 199] found that individuals with CTS were significantly shorter in stature ($P<.05$). Height of patients with CTS ranged from a mean ± standard deviation of 152.8±4.4 cm in the study by Nakamichi and Tachibana[106] conducted in Japan to 174±7 cm for Danish men in the de Krom[107] study. Mondelli et al[59] calculated the sensitivity, specificity, +LR, and -LRs using the cut off height values of ≤160.5 cm for females and ≤171.5 cm for males to differentiate those with from those without CTS. The results for the Italian women and men, respectively were sensitivity 65.5%, 56.7%; specificity 46%, 62.3%; +LR: 1.21, 1.5; and –LR: 0.76, 0.70, demonstrating poor diagnostic accuracy

Alcohol Use

III

In all 3 studies that investigated alcohol use, light to moderate drinking (< 3 drinks per day) either did not increase the risk or decreased the risk of CTS.[186, 203, 260] The results were conflicting for individuals who abused alcohol (> 3 drinks per day or binge drinking >6 drinks on 1 day).

Smoking

II/III

Studies[40, 70, 111, 243, 283] including random effects meta-analyses,[228] assessing whether there is an association between CTS and smoking provide conflicting results.

Physical Activity Level

III

Five of the 6 studies[89, 111, 116, 202, 209, 260] analyzing the effect of increased physical activity demonstrated a protective effect with OR or RR ranging from 0.40-0.97 in decreasing the risk for CTS.

Oral Contraceptive and Estrogen Use

II/III

Determining whether oral contraceptive use or estrogen replacement therapy increase the risk for CTS is complicated by the fact that more recent studies[243, 244] did not look at these medications in isolation and results of studies that separated out oral contraceptives provide conflicting results.[70, 82, 97, 111, 155, 228, 249, 250, 256, 283]

III

Studies that evaluated estrogen replacement alone demonstrated that women who underwent therapy were twice as likely to require CTR surgery than controls.[85, 266]

Women's health factors (hysterectomy, menopause, oophorectomy, parity)

Hormonal imbalance has been hypothesized as the reason for various women's factors increasing the risk of CTS. More specifically, estrogen withdrawal may have a vasodilatory action explaining menopausal hot flashes and raised pressure within the carpal tunnel.[225]

II/III

The studies that assessed the association between CTS and hysterectomy, menopause, oophorectomy and the number of births or pregnancies are conflicting.[82, 85, 92, 101, 112, 186, 191, 225, 244, 250, 270, 299]

Summary

The intrinsic risk factors with the strongest link to CTS are obesity, age, and female sex. The risk increases linearly with BMI and age. The risk doubles in individuals with BMI >30 kg/m^2 and in those over the age of 50. Female sex increases the risk between 1.5 and 4 times compared to male counterparts.

Intrinsic risk factors linked to CTS, but to a lesser extent include: diabetes mellitus, osteoarthritis, previous musculoskeletal disorders, estrogen replacement therapy, cardiovascular disease risk factors, hypothyroidism, family history of CTS, lack of physical activity, wrist ratio > 0.70, wrist-palm ratio >0.39, a short wide hand, and short stature.

No conclusion can be made on the following factors because the evidence is conflicting: rheumatoid arthritis, smoking, alcohol abuse, oral contraceptive use, menopause, parity, hysterectomy, or oophorectomy.

Occupational Risk Factors

Forceful exertions, repetitive use, vibration exposure and wrist position

I

In their prospective study to identify potential biomechanical risk factors, Harris-Adamson et al[128] found that when an individual was exposed to hand forces between 2.1 and 4 on the Borg CR10 scale (10 Categories scale with Ratio properties), the risk of CTS increased 60% and in those who rated their exposure as >4, the risk increased 117%. Increased CTS risk increased linearly with forceful hand repetition rates between rates of 2.6 to 30 per minute. However, there was no association with CTS and total hand repetition, vibration, or wrist flexed or extended posture greater than 30˚. The authors cautioned about making conclusions about vibration and wrist posture because vibration levels were not measured (simply noted to be present or absent) and the time workers were in extreme wrist postures averaged only 5.6% for flexion and 0.6% in extension. In a later analysis of this same cohort, Harris-Adamson et al[129] noted that these biomechanical risk factors were not confounded by psychosocial risk factors and vice versa.

II

All the level II studies which examined forceful exertions [49, 78, 79, 92, 141] found it to be a substantial risk factor for the development of CTS with OR or HR between 1.14 and 19.57. The risk of CTS increased linearly with increasing number of forceful exertions, with the highest HR found when exertions exceeded 60% of work time.[124] Vibration was a risk factor in 2 studies with an OR of 2.02 (95% CI 1.04, 3.9)[92] and 2.74 (95% CI 1.13, 6.65)[78] respectively. The 2 studies on extreme wrist flexion/extension positions had conflicting results.[78, 226]

III

In a meta-analysis of 9 studies of work involving non-neutral wrist posture, You et al[303] found a positive association with the development of CTS (RR = 2.01; 95% CI 1.65, 2.43). Studies using self-report of wrist postures had a higher relative risk than studies where wrist position was observed (RR = 2.95 versus 1.44).

III

Barcenilla et al[32] performed a meta-analysis of studies published between January 1980 to December 2009 relating to occupational risk factors. Based on the 37 studies, the strongest associations between CTS and occupational factors were: 1) use of vibratory tools (OR: 5.4, 95% CI 3.14, 9.31); 2) hand force (OR: 4.23, 95% CI 1.53, 11.68); and 3) repetition (OR: 2.26, 95% CI 1.73, 2.94).

Other Level III systematic reviews, case-control, and cross-sectional studies concur that use of vibratory tools,[93, 111, 123, 224, 245, 280] forceful work,[93, 112, 123, 224, 244, 263, 280] repetitive work,[111, 112, 116,

[123, 244, 245, 280] and non-neutral wrist postures,[111, 123, 163, 208, 224, 244, 263, 280] are associated with CTS. Odds ratios range as follows: 1) 1.71-14.0 for use of vibratory tools; 2) 1.5-9.0 for forceful work; 3) 0.50-9.39 for repetitive work; and 4) 1.2-8.7 for non-neutral wrist postures.

Computer use

II

Two prospective studies[189, 226] with large number of participants failed to show increased risk of CTS in those performing computer work.

II

Andersen et al[15] performed a systematic review of systematic reviews on the causal relationship between CTS and computer use. The authors concluded that epidemiological evidence for computer use and the occurrence of CTS is insufficient.

III

In their meta-analysis of studies on computer use, Shiri and Falah-Hassani[259] noted different results based on whether the control group used was composed of office workers versus individuals from the general population or other types of workers. The meta-analysis of 6 studies of office workers demonstrated a positive association between CTS and frequent computer or typewriter use (OR=1.34 95% CI 1.09, 1.65), frequent mouse use (pooled OR=1.84 95% CI 1.18, 2.8) and longer duration of computer use (OR=1.92 95% CI 1.17, 3.17). In contrast, the meta-analysis of 6 studies that compared computer workers to the general population or other types of workers, an inverse relationship was noted with computer use and CTS (OR=0.72, 95% CI 0.58, 0.90).

III

Mediouni et al[190] did not find a significant association between computer use and CTS in their meta-analysis of 6 studies, however they did not provide detail of control group composition. Mediouni et al's[190] review included only 1 study[24] that was also reviewed in the Shiri and Falah-Hassani[259] meta-analysis.

III

Al-Hashem et al[5] found a significant negative correlation (r=0.48) between the terminal latency index of the median nerve and hours of weekly mouse use. No significant association was noted between weekly keyboard use and terminal latency index (r=0.05).

V

Rempel et al[242] found significant increases in carpal tunnel pressure with typing and with wrist deviation in extension and radial deviation positioning on a keyboard when compared to static and neutral wrist positioning.

I

One systematic review[182] and 1 cohort study[127] found high decision latitude and high social support to be protective of CTS development whereas, high psychological demand increased the risk. When combining high psychological demand and low decision latitude (high job strain) the chance of developing CTS was even higher (HR=1.86 95% CI 1.11, 3.14) compared to workers with low demand and high control at work.[127]

I

However, Leclerc et al[161] did not find an association between psychological demand or social support. Additionally, the presence of somatic complaints and depression were not predictive of those with CTS. Low job satisfaction was considered a potential risk factor for women (OR=2.87 (95% CI 1.13, 7.29) but not in men.

II

Burt et al[49] concurred with level I studies that noted high job strain was associated with CTS (HR=2.13 95% CI 1.00, 4.54) in their 2-year prospective study. Other level II studies[47, 107, 226] were contradictory on whether high psychological demand and low decision authority individually were associated with CTS. Two studies supported these as risk factors and 1 found no association. Consistency at this level was found for social support at work[47, 107, 226] and job security[47, 107] with studies finding no association with these variables. Likewise, no association was found in 1 study assessing job satisfaction.[107]

III

Studies[93, 111, 160, 208, 245, 263, 280] are conflicting as to whether job dissatisfaction, job demand, job strain, and decision latitude are linked to CTS. Three studies[93, 263, 280] found no association between social support at work and CTS.

Summary
The occupational risk factor with the strongest association with CTS is forceful hand exertion. Weaker associations are present between CTS and the following factors: high psychological demand at work when paired with low decision authority, vibration, prolonged off neutral wrist positioning, and repetitive work.

Computer users do not have an increased risk of CTS when compared to the general population or industrial workers. However, when comparing office workers with short versus longer duration of computer use, the odds of CTS are only slightly increased (1<ORs <2).

DIAGNOSIS

Tests and measures used to assess individuals with complaints consistent with CTS include a symptom assessment, provocative tests, and sensory measures. An overview of each will be reported here. Both kappa (κ) values and intraclass correlation coefficients (ICCs) have been

used to report reliability data. The scale for interpreting κ values is: 0-0.20= poor, 0.21-0.40=fair; 0.41-0.60=good; 0.61-0.80=substantial; and 0.81or greater =almost perfect.[159] The scale for interpreting ICCs is: <0.40 poor, 0.41 to 0.75 fair to good, >0.75 excellent.[262]

Symptom Assessment

Katz Hand Diagram

In the Katz Hand diagram, patients are asked to indicate the location of their symptoms of pain, tingling, numbness, and/or decreased sensation on a picture of right and left hands.[146] The likelihood of CTS based on the diagram is rated as follows: 1) classic CTS: symptoms in at least 2 of 3 fingers completely innervated by the median nerve (thumb, index, or middle fingers) but no symptoms in the palm or dorsal hand; 2) probable CTS: same as classic except palmar symptoms allowed, unless only on ulnar side of the hand; 3) possible CTS: symptoms in at least one of either the thumb, index, or middle fingers; or 4) unlikely CTS: no symptoms in any of these fingers.

II

Calfee et al[51] analyzed several methods for scoring the hand diagram: 1) traditional method: using classic or probable as a positive test; 2) shading 2 or more of the volar distal surfaces of the median innervated fingers; or 3) shading the volar distal aspect of a specific median innervated finger (thumb, index, or middle). For intrarater reliability, mean kappa values were .86 for traditional scoring, .97 for using 2 or more shaded fingers, and .97 for the middle finger score. Interrater reliability improved slightly when using the middle finger score (ICC=.98) or when using 2 or more shaded fingers (ICC=.96) versus the traditional method (ICC=.87). Priganc and Henry[233] also found nearly perfect intrarater reliability for the Katz hand diagram (k=.95).

II

In a systematic review, MacDermid and Wessel[174] pooled data from 6 studies with 293 cases and 226 controls and showed sensitivity and specificity equal to 75% and 72%, respectively. Specificity increased to 90% when comparing to data from asymptomatic individuals but decreased to 60% when using data from symptomatic individuals with negative electrodiagnostic testing.

II

Calfee et al[51] prospectively examined 1107 newly hired workers from 11 companies using the Katz hand diagram, nerve conduction studies, Phalen test, and Tinel sign. The best sensitivity (67%) in comparison to the gold standard of abnormal nerve conduction was obtained using the middle finger score. Specificity, positive predictive value (PPV), and negative predictive value (NPV) were similar for all methods and ranged from 65% to 81% for specificity, 29% to 59% for PPV, and 65% to 87% for NPV. All methods were significantly associated with Phalen test but not Tinel sign. Additionally, all methods (except using the thumb alone) were good predictors of abnormal NCV. The best OR occurred when using the middle finger (OR=5.3 95% CI 2.9, 9.7). When using the traditional method, scoring the diagram as possible, probable, or classic did not change the odds of predicting those with abnormal NCV (OR: 3.3-5.5).

Provocative tests

Reliability values for provocative tests are provided in Table 2. Intrarater reliability values show good reliability for the Phalen test,[184, 233] good to substantial reliability for the Tinel sign,[184, 233] and substantial to excellent reliability for the carpal compression test.[233, 293] There was more variability in interrater reliability for these measures with κ values between .27 and .88.[171, 184, 252, 284] The Reverse Phalen test,[171] upper limb neurodynamic test (ULNT),[284] and the scratch collapse tests[41, 63] show good to almost perfect interrater reliability with κ values between .63 and .98, but these have no intrarater values available (**TABLE 2**). Sensitivity, specificity, PPVs, and NPVs are reported in **TABLE 3**.[2, 4, 9, 12, 42, 46, 63, 88, 114, 144, 157, 169, 174, 179, 185, 197, 275, 281, 282, 284, 293] Likelihood ratios were available for 4 provocative tests including Phalen,[42, 284] Tinel,[284] carpal compression,[284] and ULNT (**TABLE 4**).[46, 281, 282, 284] The following represents a brief summary of the best available evidence for Phalen test, Tinel sign, carpal compression test, Reverse Phalen, ULNT, and the scratch collapse test.

Phalen Test

I

In a systematic review of literature, MacDermid and Wessel[174] pooled data from 29 studies with more than 3000 cases and 1600 controls and showed sensitivity and specificity equal to 68% and 73%, respectively. Specificity increased to 86% when comparing to data from asymptomatic individuals but decreased to 65% when using data from symptomatic individuals with negative electrodiagnostic testing.

II

Thüngen et al[275] calculated sensitivity and specificity values using 4 different standards to confirm the CTS diagnosis (electrodiagnostics, clinical presentation, ultrasonography, and postoperative resolution of symptoms). In all circumstances, sensitivity was high (83% to 96%) and specificity was much lower (0 to 33%) than that reported by MacDermid and Wessel.[174]

II

Other studies[144, 179, 284] have also shown sensitivity ranging from 59.7% to 77% or the Phalen test, but reported variable specificity (33% to 73.9%). Wainner et al[284] examined the diagnostic accuracy of the Phalen test in 82 consecutive patients referred for an electrophysiologic examination with suspected cervical radiculopathy or CTS, and likelihood ratios (+LR=1.30; -LR=0.58) showed the Phalen test was not persuasive in changing an initial hypothesis regarding the presence of a CTS diagnosis **(TABLE 4)**.

II

Priganc and Henry[233] compared results on provocative tests to CTS severity measured by NCS. There was a significant positive trend for the Phalen test ($P<.05$) but not for the Tinel sign or carpal compression test, suggesting patients with more severe CTS are more likely to have a positive Phalen test.

IV

LaJoie et al[157] showed substantial agreement when comparing the results from NCS with results of the Phalen test (κ=0.64).

Tinel sign

I

MacDermid and Wessel[174] reported sensitivity and specificity for the Tinel sign of 50% and 77%, respectively. This conclusion was drawn based on results pooled from 27 studies including 2640 CTS cases and 1614 control subjects. Specificity decreased when using data from symptomatic individuals who had negative electrodiagnostic tests (65%) but remained higher than sensitivity.

II

Thüngen et al[275] also reported higher specificity than sensitivity (Sn=39% to 50%; Sp=65% to 100%). Additional studies reported sensitivity and specificity values.[144, 179, 284] Wainner et al[284] studied 2 variations of the Tinel test. In the first (Tinel A), a reflex hammer, held 15 cm above the patient's wrist crease, was allowed to fall and strike the patient between the tendons of the flexor carpi radialis and palmaris longus, with a positive test being non-painful tingling sensation radiating distally along the path of the median nerve. In the second test (Tinel B), the examiner tapped the patient with reflex hammer using mild-to-moderate force in the same location attempting to reproduce symptoms. In Tinel B, positive test criteria included discomfort or pain at the wrist or radiating distally along the nerve's course. Likelihood ratios indicated the Tinel test results would provide negligible change from pre- to post-test probability (Tinel A: +LR=.98, 95% CI .56, 1.7; –LR=1.0 95% CI .69,1.5; Tinel B: +LR=1.4, 95%CI .84, 2.5; –LR=.78 95% CI .52, 1.2) **(TABLE 4).**

IV

LaJoie et al[157] showed substantial agreement when comparing the results from NCS with results from the Tinel sign (κ=0.71).

Carpal Compression test

II

Sensitivity and specificity values reported for the carpal compression are reported in **TABLE 4**.[8, 88, 114, 144, 169, 174, 179, 197, 275, 284, 293] The review by MacDermid and Wessel[174] (classified as a Level II based on the quality of 17 studies reviewed for the carpal compression test) showed higher specificity than sensitivity (Sp=83%; Sn=64%) when using data from asymptomatic controls. When using data from symptomatic individuals with negative electrodiagnostic tests, specificity decreased to 64%.[174] Likelihood ratios show negligible changes in pre- to post-test probability for the carpal compression test.[284]

Reverse Phalen test

II

According to the MacDermid and Wessel[174] systematic review, the Reverse Phalen test has higher specificity (78%) than sensitivity (57%) values.

IV

Goloborod'ko[114] also reported very high values for both sensitivity (88%) and specificity (98%) after examining 34 patients (41 hands).

Upper Limb Neurodynamic Testing

I/II

Studies on the sensitivity, specificity, PPVs, NPVs, and likelihood ratios of ULNT1 are reported in **TABLES 3 and 4**.[46, 281, 282, 284] In these studies, +LRs range from 0.86 to 3.67 for ULNT1 and –LRs range from 0.75 to 1.90. Studies used different criteria for what was considered a positive test **(TABLE 4)**.

II

Baselgia et al[33] examined the ULNT1 and ULNT2a to determine the presence of a positive test in those with and without CTS using electrodiagnostic testing as the reference standard. Authors also compared results of ULNT to quantitative sensory testing. In individuals with electrodiagnostically-confirmed CTS, only 46% had a positive ULNT. Those with negative ULNT demonstrated greater dysfunction in the unmyelinated nerve fibers according to findings on the quantitative sensory testing.

Scratch collapse test

II

There were 2 level II studies documenting sensitivity and specificity for the scratch collapse test, providing conflicting results (**TABLE 3**).[63, 179]

Sensory measures

Sensory testing has been advocated in the diagnosis of CTS to determine the extent of nerve injury. Hypoxia (as thought to occur in CTS) is proposed to affect large diameter nerve fibers earlier than small diameter fibers, so sensory tests, which stimulate large A-beta fibers would, theoretically, be able to detect CTS in the early stages.

Results from studies on reliability and diagnostic accuracy of sensory instruments are reported in **TABLES 5 through 7**.[60, 68, 108, 126, 139, 171, 172, 174, 183, 184, 275, 292, 301] Testing with the PCV50 computerized vibrometer (Z tech Medical, Salt Lake City, UT) demonstrated excellent intrarater reliability. However, this instrument may not be available for clinicians. There were no studies

on the reliability of current perception threshold testing, and therefore it is not included in the discussion. Main findings from studies are summarized below.

Semmes Weinstein Monofilaments

I

Following a systematic review, average sensitivity was 72% with specificity 62% (86% when comparing to asymptomatic controls and 70% when comparing to those with symptoms and negative electrodiagnostic findings).[174]

II

Yildirim and Gunduz[301] reported the greatest sensitivity (98%) occurred when any radial finger tested higher than the 2.83 filament, but the greatest specificity (97%) when using the 3.22 filament as the threshold for normal and comparing middle finger sensation to that of the small finger. However, the highest diagnostic accuracy (76%) occurred when any radial finger tested higher than 3.22. In patients with moderate-to-severe CTS, the best diagnostic accuracy (90%) resulted when any radial finger tested higher than 3.22.

IV

Studies on the correlation between Semmes Weinstein monofilament testing (SWMT) and nerve conduction study results are conflicting. Raji et al[236] found moderate correlations using the monofilament values taken from the thumb (r_s=-0.42, 0.44, and 0. 44 for SDL, sensory amplitude, and NCV, respectively). Correlation coefficients using data from other fingers did not exceed 0.33, and only 52% of patients with positive NCS also had abnormal SWMT findings when the 2.83 monofilament was used as the threshold for normal. Elfar et al[90] found no significant correlation between SWMT and electrodiagnostic studies (correlation values not provided, P>.05) using data from the middle finger.

Static Two-Point Discrimination

I/II

Results from 1 Level I and 1 Level II study showed that 2PD has higher values for specificity than sensitivity suggesting it would be more valuable for diagnostic confirmation (**TABLE 5**).[108, 275]

III

The systematic review by MacDermid and Wessel[174] also showed higher specificity than sensitivity. Wolny et al[296] compared the results of 2PD testing in 100 people with a clinical diagnosis of mild or moderate CTS. Results showed a significant difference in 2PD scores tested at the radial 3 fingers between symptomatic and asymptomatic fingers; however, mean 2PD scores were 6 mm and less, which is the accepted normal value for 2PD.

IV

Elfar et al[90] showed the middle finger was the most involved finger in CTS when examining 2PD scores. Using data from the middle finger, they compared 2PD results with electrodiagnostic testing and found a moderate correlation (r=.42, P=.0003). There was no significant correlation between 2PD and electrodiagnostic tests for the other fingers.

Vibrotactile Testing

Vibration is perceived via different receptor types (slow versus fast adapting) with varying receptive borders (small and sharp versus ill-defined). Slowly adapting receptors include: 1) Merkel cells which respond to vibration frequencies of .4 to 2 Hz and have sharp receptive fields and 2) Ruffini end organs which respond to frequencies of 100 to 500 Hz, but have ill-defined receptive fields. The fast adapting receptors with sharp receptive fields are Meissner's corpuscles which are stimulated by vibration frequencies of 2-40 Hz. Pacinian corpuscles are also fast adapting, responding to frequencies of 40 to more than 500 Hz, but have ill-defined receptive fields.[60, 167] Based on this physiology, vibration testing at different frequencies could provide different information in the diagnosis of CTS. Findings from studies on the reliability, diagnostic accuracy, and known-group validity of vibrometry in CTS are reported in **TABLES 6 and 7**. Results of studies on concurrent validity are described below. There is a lack of consistent findings in the relationship between vibration sense and NCS because authors have compared various frequencies and various aspects of nerve conduction.

I

Werner et al[292] evaluated testing frequencies of 8, 16, 32, 63, 125, 256, and 500 Hz. Authors reported statistically significant relationships between vibration sense and median sensory peak and amplitude but the magnitude of the correlation coefficients were weak (r=.02-.32). In addition, these authors did not find any significant differences in vibration sense in those with CTS compared to a control group at 16, 32, 125, 250, or 500 Hz. There were differences at 8 and 63 Hz, but in another Level I study, Checkosky et al[60] found a difference in CTS cases and controls at 10 Hz but no differences at 1 or 300 Hz.

III

In a systematic review, MacDermid and Wessel[174] found the sensitivity and specificity for the 256 Hz tuning fork were 55% and 81%, respectively.

Combining individual tests into test batteries

II

Wainner et al[284] showed a balance between sensitivity (0.98) and specificity (0.54) with more than 3 positive tests from the following: shaking hands relieves symptoms, wrist-ratio index >0.67, CTQ-SSS>1.9, diminished sensation in median nerve distribution, and age >45 years. Requiring all 5 to be positive decreased sensitivity to 0.18 and increased specificity to 0.99. The greatest +LR (4.60 95% CI 2.5, 8.7) occurred when 4 or more of these tests were positive (**TABLE 4**).

III

Ntani et al[210] examined results from 1806 hands in 908 individuals. Sensory NCV was most diminished in hands with: 1) extensive numbness or tingling in the median nerve sensory distribution and 2) a positive Tinel sign and Phalen test. The authors recommended combining the Tinel sign and Phalen test to serve as diagnostic filters. When patients demonstrated a negative Tinel sign and Phalen test, there was no need to refer the patient for sensory nerve conduction testing. The authors did not report sensitivity and specificity values, based on reasoning that no measures, including electrodiagnostic testing, could be considered a valid gold standard.

IV

Four studies supported the value of combining singular tests into a test battery to improve diagnostic accuracy. Koris et al[153] included patients with confirmed CTS and individuals without CTS and found that combining results across fingers from SWMT increased sensitivity from 16% to 82%, with specificity equal to 86%. Fertl et al[98] examined 47 patients (63 hands) with CTS confirmed by NCS and 20 healthy controls (39 hands) and found that combining a timed Phalen test (timed to appearance of symptoms) and the manual carpal compression test improved all diagnostic statistics resulting in a PPV of 95% and a NPV of 88%. In a retrospective, unblinded chart review, LaJoie et al[157] reviewed data from 81 patients (162 wrists). Outcome measures were Tinel sign, Phalen test, and NCS findings. When all 3 tests are positive, the probability of having CTS was 99%; when Tinel and Phalen were positive probability was 92%, when Tinel and NCS were positive probability was 93%; and when Phalen and NCS were positive probability was 68%. The authors concluded that when one of the provocative tests is positive and the other negative, there is a large potential gain in probability of disease with positive findings from NCS. When both clinical tests are negative or both are positive, there is little gain from performing NCS. Boland and Kiernan[42] examined 86 hands (74 hands with electrophysiological changes and 12 without) and found that the addition of sensory testing using the pinprick testing tool does not improve the diagnostic accuracy for the Phalen test or modified carpal compression test.

Evidence Synthesis and Clinical Rationale

There is variability in the methods used in studies examining accuracy of diagnostic tests for CTS. This makes it difficult to compare study results and arrive at a recommendation for one preferred test. Variability can be attributed to differences in research designs, study settings, reference gold standards used for confirming the CTS diagnosis, and test performance and interpretation. Also, the majority of studies used asymptomatic control groups leading to diagnostic results distinguishing patients with CTS from non-patients, whereas a lesser number of studies used individuals with other upper extremity pathologies, leading to clinically relevant differential diagnosis. While diagnostic accuracy values for some aforementioned tests may be acceptable, there is no evidence to support an isolated test or measure that can confirm the presence of CTS. The greatest likelihood ratios were found when subjective and/or objective data were combined with anthropometric measurements[98, 157, 284]; however, these data need further validation in separate and larger samples.

Gaps in knowledge

Additional research is needed to determine how these tests can help clinicians assess the presence and severity of CTS as well as differentiate CTS from other UE compression neuropathies. There is insufficient evidence available to determine the usefulness of the finger flexion wrist flexion with compression test, flick test, Luthy sign, lunate press test, modified carpal compression (that used oscillations over carpal tunnel) test, modified pneumatic compression test, Tanzer test, tethered median nerve tests, current perception threshold tests, and moving 2PD test.

Recommendations

A

When examining a patient with suspected carpal tunnel syndrome (CTS), clinicians should use Semmes Weinstein monofilament testing (SWMT) using the 2.83 or 3.22 monofilament as the threshold for normal (better specificity with the 3.22). In those with suspected moderate-to-severe CTS, clinicians should assess any radial finger using the 3.22 filament as the threshold for normal. SWMT testing should be repeated by the same provider because the intrarater reliability is better than interrater reliability. Clinicians should also use static 2-point discrimination on the middle finger in their examination of individuals with suspected CTS.

B

In those with suspected carpal tunnel syndrome, clinicians should use the Katz Hand Diagram, Phalen test, Tinel sign, and carpal compression test and interpret examination results in the context of all data. Clinicians should also assess: patient age (>45 years), whether or not shaking hands relieves symptoms, sensory loss in the thumb, wrist-ratio index (>.67), and scores from the Carpal Tunnel Questionnaire-Symptom Severity Scale (>1.9) because the presence of more than 3 of these clinical findings has shown acceptable diagnostic accuracy.

D

There is conflicting evidence on the diagnostic accuracy and clinical utility of the upper limb neurodynamic tests, scratch-collapse test, and tests of vibration sense in the diagnosis of carpal tunnel syndrome, and therefore no recommendation can be made.

CLINICAL GUIDELINES:
Examination

OUTCOME MEASURES:
ACTIVITY LIMITATIONS/SELF-REPORTED MEASURES

Boston Carpal Tunnel Questionnaire Symptom Severity Scale (CTQ-SSS)

II

The Boston Carpal Tunnel Questionnaire Symptom Severity Scale (CTQ-SSS) is an 11-item questionnaire used to assess symptom severity in individuals with CTS. Each item is scored on a Likert scale from 1 to 5 (5 being worst), with the patient's CTQ-SSS score being the average score of all items. Final scores can range from 1 (no symptoms) to 5 (worst symptoms). Internal consistency,[30, 162] test-retest reliability,[10, 30, 119, 162] and validity (construct and concurrent),[19, 30, 102, 162] have been reported in multiple studies and are excellent. CTQ-SSS scores have shown weak to no correlation with NCS,[30, 84, 162] but it has demonstrated higher sensitivity to change than any other outcome measure in individuals following surgery at 6 weeks,[30, 102] 3 months,[7, 23, 102, 119] 4 months,[138] 6 months,[19, 59] 8 months,[138] and 14 months.[162] The CTQ-SSS has also been shown to be responsive in individuals following 6 weeks of orthosis management[65] and 3 weeks following cortisone injection.[220]

II

Conflicting results have been published on the predictive and discriminant validity of the CTQ-SSS. Baker and Livengood[27] reported that baseline score was a significant predictor of progression to surgery in patients without atrophy in the thenar muscles (OR= 12.5 95% CI 3.1, 50.7), and Boyd et al[44] concluded that baseline CTQ-SSS was the best predictor of failed non-surgical management when compared to the Boston Carpal Tunnel Questionnaire Functional Scale (CTQ-FS), the Disabilities of the Arm, Shoulder, and Hand (DASH), the Short-Form 36 Health Survey, grip strength, dexterity, and sensory threshold. Ollivere et al[213] found the CTQ-SSS was the best predictor of success with non-surgical management in that baseline scores less than 2.5 were 89% specific for success. Kaye and Reynolds[147] reported that people with a mean CTQ-SSS score of 3.0 had a 72% probability of progression to surgery and a score of 3.5 had an 86% probability. However, Gerritsen et al[110] identified the CTQ-SSS as a predictor of outcome at 12 months in a single variable analysis, but the measure did not remain significant when placed into a multiple logistic backward regression model. Reported values for the minimal clinically important difference (MCID) for the CTQ-SSS are reported in **TABLE 8**.

II

One study investigated the factor structure of the CTQ-SSS.[25] Following factor analysis, authors suggested shortening the original 11-item instrument to a 6-item instrument (CTQ-6).[25, 26, 168] The internal consistency (Cronbach alpha=0.86) and test-retest reliability (ICC=.95 95% CI .90, .98) of the 6-item instrument were excellent.[25] Correlation with the original, 11-item instrument was .80 (95% CI .73, .86) and correlation with QuickDASH was .87 (95% CI .82, .91).[25] Responsiveness for the CTQ-6 evaluated within a year following carpal tunnel release surgery was excellent (ES=2.03 for all patients and 2.53 for those reporting Large Improvement).[26] The MCID is 0.90.[25, 26, 168] The instrument also discriminated between different levels of change and patient satisfaction.[25] However, there are no data on the CTQ-6 on patients managed non-surgically, and it has not been independently validated outside the original authors.

Boston Carpal Tunnel Questionnaire-Functional Scale (CTQ-FS)

II

The CTQ-FS is an 8-item questionnaire to assess the functional status of patients with CTS. Each item is scored on a Likert scale from 1 to 5 (5 being worst), with the score being the average of

all 8 items. Final scores can range from 1 (no functional deficits) to 5 (worst function possible). Internal consistency,[30, 162] test-retest reliability,[10, 30, 119, 162, 233] and validity (construct and concurrent)[30, 102, 162, 164] have been reported in multiple studies and are excellent. The CTQ-FS has shown no correlation with NCS.[30, 162]

Disabilities of the Arm, Shoulder, and Hand (DASH)

II

The DASH is a 30-item questionnaire designed to assess disability in patients with upper extremity pathology. Measurement properties, including internal consistency,[134] reliability,[10, 30, 119] and validity,[30, 102, 134] are well documented in patients with CTS and are excellent. Bakhsh et al[30] showed a high correlation between the CTQ-FS and the DASH. The DASH has shown no correlation with NCS.[30]

II

Responsiveness and MCID of the CTQ-FS, DASH, and QuickDASH have not been evaluated in those undergoing non-surgical management. Neither the CTQ-FS nor the DASH were able to predict progression to surgery.[44] Post CTR surgery, the CTQ-FS,[10, 19, 30, 59, 102, 119, 138] DASH,[10, 30, 102, 119, 134, 154, 188] and QuickDASH[26, 168] have been shown responsive to change and values are similar, ranging from moderate to high.[7, 119, 134, 305] Responsiveness values for the CTQ-FS and DASH are lower than those for the CTQ-SSS.[102, 119] Bessette et al[38] reported the MCID for the CTQ-FS at 6 months post-surgery was .74. Ozer et al[217] reported the MCID for the CTQ-FS was 1.95 for individuals with diabetes and 1.25 for those without (also evaluated 6 months post-surgery). The MCID for the DASH reported at 6 weeks post CTR surgery was 21%.[10] Amirfeyz et al[10] reported the MCID at 6 weeks post-surgery for the CTQ-SSS and CTQ-FS post-surgery were .16 and .47, respectively. The total score from the CTQ-SSS and CTQ-FS has also been shown to be responsive following surgery.[38, 102]

QuickDASH

III

The test-retest reliability for the QuickDASH ($ICC_{2,1}$ .69; 95% CI .43, .84)[264] is lower than the CTQ-SSS, the CTQ-FS, and the DASH. The correlation between QuickDASH scores and electrodiagnostic findings is not statically significant (rho-.18; P=.08).[277]

Evidence Synthesis and Clinical Rationale

Psychometric properties of the CTQ-SSS, CTQ-FS, and the DASH are excellent. There is more evidence available on those undergoing surgical management and only limited evidence on those undergoing non-surgical management. Only the CTQ-SSS has been shown to be responsive to change in those undergoing conservative management.

Gaps in Knowledge

More research is needed to validate the shorter version of the CTQ-SSS and to examine the psychometric properties of the functional measures in patients with CTS undergoing non-surgical management. While higher baseline CTQ-SSS scores have shown to predict progression to CTR surgery in some studies,[44, 147] further validation in larger, independent samples is needed.

Recommendation

B

Clinicians should use the CTQ-SSS to assess symptoms and the CTQ-FS or the DASH questionnaire to assess function when examining patients with CTS. Clinicians should use the CTQ-SSS to assess change in those undergoing conservative management.

ACTIVITY LIMITATIONS/PHYSICAL PERFORMANCE MEASURES

While activity limitations and participation restrictions can be evaluated in part using self-report measures, there are data available on patient-performance measures including the Purdue Pegboard (PPB), the Dellon-modified Moberg Pick-up Test (DMPUT), the Jebsen-Taylor Hand Function Test, and the Nine-Hole Peg Test in individuals with CTS.

Purdue Pegboard

III

Normative data for the PPB test exist.[1, 83, 300] Test-retest reliability as a measure of dexterous hand function in individuals with CTS has been reported in a sample of 51 individuals (20-86 years old) with electrophysiologically-confirmed CTS and is excellent (ICC=.97).[12] The PPB discriminates between those with and without CTS in individuals 66 years old and under.[80, 95]

III

Amirjani et al[12] included people with CTS aged 20 to 86 years old and found decreased PPB test scores in young (ages 20-39 years) and middle-aged (40-59 years) participants compared with controls, but in the elderly (ages 60+), there was only a difference in participants with moderate and severe CTS. Authors concluded that performance on the PPB declines with age regardless of carpal tunnel pathology.[12] Atalay et al[20] found lower PPB subtest scores in those with severe CTS compared to those with mild disease.

III

When compared to NCS, there were no meaningful associations between PPB test scores and DSL or DML ($r<.15$; $P>.05$),[80] or between PPB test scores and the total CTQ score for younger individuals ($r<.22$; $P>.05$).[12] The correlations between the subtests of the PPB and CTQ scores for individuals 60 and older were higher ($r=.33$ to $.45$; $P<.05$).[12] PPB test scores have moderate-to-high correlations ($r=-.50$ to $-.76$; $P<.001$) with pain duration and severity.[95]

III

There is conflicting evidence on the ability of the PPB to discriminate between individuals with different CTS severities. de la Llave-Rincón et al[80] found no difference in scores of all PPB subtests in individuals with mild, moderate, or severe CTS, while Atalay et al[20] reported a significant difference in PPB scores between individuals with mild CTS and those with severe CTS, but only for the dominant hand. Lastly, authors have reported bilateral deficits in fine hand use measured by the PPB in patients with unilateral mild-to-moderate CTS.[95]

II

Olsen and Knudsen[214] examined recovery of fine hand use using the PPB in 11 patients, 5 months following CTR surgery using trend analysis. Recovery followed a linear path with a flat slope, suggesting that surgery did not result in a marked improvement in PPB scores even though the preoperative scores were well below normal.

Dellon-modified Moberg Pick-up Test

III

Normative data for the DMPUT have been reported for 116 individuals 20 years and older and indicate better performance for women compared to men and declining performance with age.[11] Test-retest reliability in patients with CTS has been reported in a sample of 46 individuals with electrophysiologically-confirmed CTS and is excellent (ICC=.91 95% CI 0.87, 0.95).[13] For known-group validity, authors found significant differences in scores between those with and without CTS suggesting the DMPUT is useful in discriminating between those with and without CTS. However, when stratifying by age, the authors found similar scores in the elderly individuals with mild CTS and the control group.[13]

II

Appleby et al[16] reported a statistically significant change in DMPUT scores in 29 patients tested before and 12 weeks following CTR surgery. Using the means and standard deviations reported in the study, responsiveness could be calculated (standardized response mean (SRM)=.90 and ES=.71) suggesting the DMPUT is acceptable at assessing change following surgery. There are no data on the responsiveness of the DMPUT in individuals undergoing non-surgical management.

Jebsen-Taylor Hand Function Test and Nine-Hole Peg Test

II

Sears and Chung[255] examined the responsiveness of the Jebsen-Taylor Hand Function Test and reported it was a poor indicator for improvement after CTR surgery (ES=.05; SRM=.04). Hobby et al[134] studied responsiveness of the Nine-Hole Peg test following CTR surgery and found this measure was also not responsive to change (ES=.16; SRM=.12). There are no data on these measures for individuals undergoing non-surgical management.

Evidence Synthesis and Clinical Rationale

Norms are available for both the PPB and the DMPUT. While the PPB test discriminates between those with and without CTS aged 60 and under, it is not useful in monitoring progress after CTR surgery. The DMPUT also discriminates between those with and without CTS in younger patients and can help in assessing change following CTR surgery because data presented on responsiveness of this instrument are from individuals who underwent CTR surgery.

Gaps in knowledge

More research is needed on the responsiveness of all physical performance-based measures in individuals with CTS undergoing non-surgical management.

C

Clinicians may use the Purdue Pegboard (PPB) or the Dellon-modified Moberg Pickup Test (DMPUT) to quantify dexterity at the onset of treatment and compare scores with established norms. Clinicians should not use the PPB test, Jebsen-Taylor Hand Function Test, and the Nine-Hole Peg Test to assess clinical change following CTR surgery. Clinicians may use the DMPUT to assess change.

ACTIVITY LIMITATIONS/PHYSICAL IMPAIRMENT MEASURES

Strength measures

II

For predictive validity, Boyd et al[44] reported no significant difference in grip strength between individuals with CTS who progressed to surgery and those who did not. Studies on sensitivity-to-change of grip strength have been done following CTR surgery. In those studies, grip strength was not sensitive to change over time.[7, 19, 134, 138, 145, 231] Following surgery, grip strength actually decreases and doesn't begin to increase until the third post-operative month.[103, 305]

II

Lateral pinch is not sensitive to change following CTR surgery.[103] Additionally, lateral pinch receives motor input from median and ulnar-innervated muscles making it an invalid measure in individuals with CTS.[103] While tip and three-point pinch both target more median-innervated muscles, there are no data on the sensitivity-to-change of tip or three-point pinch in patients managed non-surgically. There is conflicting evidence on the sensitivity-to-change of tip and three-point pinch following CTR surgery.[103] Existing data on assessment of APB muscle strength from patients following CTR surgery also present conflicting results.[103, 138, 145]

III

Reliability of strength measures in patients with CTS including grip,[6, 73] tip pinch,[95] three-point pinch,[6] and lateral (key) pinch[6] is >.81. For grip strength, reliability is best when using a single trial or using the highest score of 3 trials.[73] Known-group validity has also been studied in this population.[28, 95] Significant differences in grip strength, three-point pinch, lateral pinch,[28] and tip pinch[95] have been found between those with and without CTS. Atalay et al[20] reported significant differences in tip and three-point pinch between those with mild and moderate CTS compared to those with severe CTS but no differences in grip strength.

Evidence Synthesis and Clinical Rationale

Lateral pinch receives dual innervation from the median and ulnar-innervated muscles making it unacceptable as a measure in CTS. Tip and three-point pinch receive innervation from more median-innervated muscles but there is innervation from branches proximal and distal to the carpal tunnel. The available evidence on the value of tip and three-point pinch in the assessment of individuals with CTS is conflicting. Evidence on strength testing of the APB muscle is also conflicting.

Gaps in Knowledge

There are no data on the sensitivity to change of instruments to assess strength in individuals with CTS being managed non-surgically. All available data are on individuals being managed with CTR and suggest that strength measures are not useful in these individuals. However, due to the presence of a post-surgical wound/scar, one should not expect to apply these results for patients managed non-surgically. Also, there is conflicting evidence on the presence of grip strength weakness in individuals with CTS and there is a need for more research in this area.

Recommendations

B

Clinicians should not use lateral pinch strength as an outcome measure for patients with non-surgically or surgically managed carpal tunnel syndrome.

B

Clinicians should not use grip strength when assessing short-term (< 3 months) change in individuals following carpal tunnel release surgery.

D

There is conflicting evidence on the use of tip and three-point pinch strength and APB muscle strength testing in individuals following CTR surgery.

Sensory and Provocative measures

II

There are no studies assessing sensitivity-to-change of static 2PD in patients undergoing non-surgical management for CTS. There were 5 studies using the interpretation provided by Cohen's criteria (small d = 0.2, medium d = 0.5, large d = 0.8)[71] following CTR with conflicting results. Authors of 4 studies reported small-to-medium ES at 1, 3, 4, and 8 months after CTR surgery (0.39, 0.51, 0.22, and 0.33, respectively).[134, 135, 138, 145] Authors of a lower-quality study reported a large ES of 0.88 at 18 weeks following surgery.[134] Other authors found low-to-moderate SRMs at 3, 4, 6, and 8 months after surgery (0.10-0.59, 0.57, 0.30, and 0.51, respectively).[22, 134, 138, 145] There was 1 study on the sensitivity-to-change of moving 2PD following CTR (ES=0.44) at 1 month following surgery.[135]

II

There is only 1 study on the responsiveness of threshold testing in individuals undergoing non-surgical management.[65] Authors used both distribution-based methods to assess sensitivity-to-change, and anchor-based methods for determining responsiveness of the Pressure Specified Sensory Device (PSSD) in individuals treated with an orthosis for 6 weeks. Results indicated low sensitivity-to-change (ES<.08 and SRM <.09) for those who responded to treatment as measured by change score on the CTQ-SSS. Based on the receiver operating curve (area under the curve= .46), authors concluded the instrument did not discriminate between those who improved and those who did not. Five studies reported low-to-moderate sensitivity for threshold testing following CTR surgery. ES values were .76 (1-month post CTR),[135] .41 (3-months post CTR),[145] .55 (4 -months post CTR), and .73 (8-months post CTR).[138] Standardized response means were .30 to .70 (3-months post CTR),[7, 22, 145] .59 (4-months post CTR),[138] and .60 (6-months post CTR).[22] The highest quality study reported a large SRM (.84) at 8-months post release.[138] These values are lower compared to ESs and SRMs reported for the CTQ-SSS which exceeded 1.0 in many of the same studies.[7, 22, 138, 145]

II

Vibration sense before and after intervention has been evaluated using a tuning fork and different vibrometers. There is no evidence on the sensitivity or responsiveness of using a tuning fork in those undergoing non-surgical management. There is only 1 study on the sensitivity-to-change of vibration sense measured using a 50-hz computer-controlled vibrometer in individuals undergoing non-surgical management.[65] Cheung et al[65] reported moderate sensitivity using the vibrometer in those that responded to treatment (ES=.46 95% CI .05, 0.47; SRM=.61 95% CI=.20, 1.02). However, these authors concluded that their results did not provide sufficient evidence that it was useful for clinical decision making in determining whether a clinically important difference occurred.

II

Pransky et al[231] assessed sensitivity to change in self-report, impairment, and provocative measures in a group of patients post CTR surgery who reported improvement (average follow-up 18 months). Phalen test was more sensitive to change (SRM=.92) than grip (SRM=.38) or pinch strength (SRM=.39).

Evidence synthesis and clinical rationale

For 2PD and SWMT, there is conflicting evidence on the sensitivity to change following CTR surgery. Data available for threshold and vibration sense are limited and do not support use of these measures.

Gaps in knowledge

There is no evidence available for using 2PD and provocative measures in individuals with CTS managed non-surgically. The use of the Phalen test to assess change in CTS needs further validation.

Recommendations

C

Clinicians should not use threshold or vibration testing to assess change in individuals with CTS undergoing non-surgical management until more evidence becomes available. Clinicians may use the Phalen test to assess change in those with carpal tunnel release surgery at long-term follow-ups.

D

There is conflicting evidence on the use of sensory measures including 2-point discrimination and threshold testing to assess change over time in patients with surgically managed CTS.

CLINICAL GUIDELINES: Interventions

ASSISTIVE TECHNOLOGY

Computer Component Design

The benefits attributed to ergonomically-designed computer equipment include: 1) reduction of carpal tunnel pressure[104]; 2) alignment of the wrist in the position that maximizes the space in the carpal tunnel[211]; 3) reduction of the work of the tendons within the carpal tunnel through reduced force output[241]; 4) reduction of the velocity and frequency of relative sliding between the contents of the carpal tunnel[99, 151]; and 5) reduction of finger flexion range of motion thereby preventing migration of the extrinsic or intrinsic muscle bellies into the carpal tunnel.[69]

II

In a Cochrane review, O'Connor et al[211] analyzed 2 randomized placebo-controlled trials evaluating the effectiveness of ergonomic keyboards.[211, 240] Rempel et al[240] compared self-reported pain level, symptom relief, hand function, and NCS in individuals with CTS (all severities) using an ergonomic keyboard to those using a standard keyboard for 6 and 12 weeks. Both keyboards included a conventional layout but differed in the required force needed for key displacement. Rempel et al[240] found improvement in pain levels between 6 and 12 weeks for those in the reduced key strike force group (weighted MD [WMD]: -2.40, 95% CI -4.45, -.35).[211] Tittiranonda et al[276] compared pain severity in 80 individuals with CTS (unspecified severity) using one of 3 ergonomic keyboards or a standard keyboard and found no significant difference in pain severity at 6 months compared to baseline. Neither study reported adverse effects associated with the use of the keyboards. O'Connor et al[211] concluded there was insufficient evidence for or against the short or long-term effectiveness of the studied ergonomic keyboards in patients with CTS.

II

Schmid et al[254] compared the effects of a vertical mouse, a standard mouse used with a gel mouse pad, a standard mouse used with a gliding palm support, and a standard mouse alone on carpal tunnel pressure, wrist angle, and comfort level in 21 individuals with mild or moderate CTS during a 5-minute mouse task. Authors reported a significant increase in carpal tunnel pressure during the mouse task for all 4 conditions compared to baseline (MD=20 mmHg; P<.0001). For wrist angle, the gel mouse pad and pad with gliding palm support decreased wrist

extension-flexion angles compared to the standard mouse (P<.003) but did not change radio-ulnar deviation angle (P>.07). The vertical mouse showed the largest extension angle (P<.0001) but the smallest ulnar deviation angle (P<.006). There was no difference in patient-reported comfort across the 4 devices (P=.71). Schmid et al[254] concluded there was insufficient evidence to make recommendations for or against any of the devices.

Evidence Synthesis and Clinical Rationale
Ergonomic devices are more expensive than standard devices.[211] There is insufficient evidence to support the use of the studied ergonomic keyboards, mice, or mouse pads to reduce risk of developing CTS. Evidence does suggest that mouse use increases carpal tunnel pressure in all the studied mouse designs. As noted earlier in this guideline, increased carpal tunnel pressure above 30 mm[166] and forceful hand exertions are strongly associated with CTS.[128]

Gaps in Knowledge
High-quality studies to evaluate the effectiveness of non-standard keyboards, mice, and mouse pads using valid, reliable, and responsive outcome measures in individuals with CTS are needed. More studies are needed to identify equipment designs justifying the additional expense.

Recommendation

C

Clinicians may educate their patients regarding the effects of mouse use on carpal tunnel pressure and assist patients in developing alternate strategies including the use of arrow keys, touch screens, or alternating the mouse hand. Clinicians may recommend keyboards with reduced strike force for patients with CTS who report pain with keyboard use.

ORTHOSES

The rationale for using static wrist orthoses for individuals with CTS is based on several theories including: reducing tendon and nerve movement through the carpal tunnel and thereby reducing inflammation; immobilizing the wrist in the position of least internal pressure in the carpal tunnel; altering the shape or dimensions of the tunnel to increase space; reducing tunnel contents by positioning the wrist and fingers to prevent the lumbrical muscle origins from migrating proximally into the carpal tunnel or prevent the proximal muscles from advancing distally.[76, 87, 148, 239]

In a Cochrane review, Page et al[222] reviewed 19 studies published before January 2012. They performed sub-analyses on the effectiveness of orthoses versus no intervention, orthoses versus other non-surgical interventions, and orthosis design and position. The review also reported on the combined effects of orthoses and steroid injection, orthoses and NSAIDs, and orthoses and ergonomic education. The results of the sub-analyses are included below in addition to studies published after the Cochrane Review.

Orthosis versus No Intervention

II

Page et al[222] reviewed 2, level 2 studies comparing orthosis use to no intervention. Manente et al[181] evaluated 80 individuals using a soft, hand-based support at night. Use of the support for 4 weeks resulted in short-term symptom improvement in the CTQ-SSS (MD=-1.07 95% CI -1.29, -0.85) and the CTQ FS (MD=-0.55 95% CI -0.82 to -0.28).[222] Page et al[222] concluded that the orthosis group was more than 3 times as likely to report improvement than the no-orthosis group (RR 3.86; 95% CI 2.29, 6.51). Premoselli et al[232] evaluated symptom and functional improvement in 50 wrists at 3 (n=48) and 6 months (n=34) following use of a custom-fabricated, volar, neutral wrist orthoses worn at night compared to no intervention. At 3 months, the difference in scores between the orthosis group and the control favored the orthosis group on the CTQ-SSS (MD=– 0.94 95% CI -1.10, -0.78) and the CTQ-FS (MD=-0.22 95% CI -0.40, -0.04).[222] At 6 months, the difference between groups persisted on the CTQ-SSS (MD=-0.90 95% CI -1.11 to -0.69) and CTQ-FS (MD=- 0.2 5 95% CI -0.68, 0.18). Results from the NCS parameters were conflicting. Page et al[222] concluded the precision of the effect estimates was low and both studies were determined to have a high risk of bias. Adverse effects were reported in the orthosis group in the Manente[181] study which included difficulty falling asleep (3/40 individuals) and transient morning paresthesias (4/40 individuals).

Orthosis Design and Position

Orthosis design includes material (cloth, thermoplastic, plaster), limb placement (volar, dorsal or ulnar) and the specific joints included in the orthosis (wrist, thumb, MP joints, IP joints). Orthosis position describes the angle of immobilization of the included joints.

II

Page et al[222] analyzed 5 Level II studies comparing orthosis design and position including wrist immobilization ranging from 30° of extension to neutral, inclusion of MP joint immobilization, and/or thumb immobilization. They concluded there was insufficient evidence to recommend one design or position over another.

Wrist position

IV

Özgen et al[218] used sonography to determine the immobilization position associated with the greatest median nerve area for 21 individuals (37 wrists) with idiopathic CTS of all severity levels. Median nerve dimensions in the carpal tunnel were taken in 4 wrist positions. The results showed individual variation. Forty-three percent of wrists showed the greatest median nerve area at 15° of wrist flexion, 32% at 0°, 16% at 15° of extension and 8% at 30° extension. Participants were immobilized in the position that demonstrated their greatest median nerve dimension for 6 weeks with a custom-fabricated volar wrist orthosis. Outcome measures included CTQ-SSS, CTQ-FS, pinch strength, and grip strength. The participants positioned in 30° wrist extension were eliminated due to the small group size and were not accounted for in the final analysis. The remaining 3 groups demonstrated significantly improved CTQ-SSS scores ($P \leq .05$). For the CTQ-FS, only the wrist flexion group demonstrated a significant improvement (MD=-3.0; $P < .05$), and for grip strength, only the neutral position group demonstrated significant improvement (MD=1.85 kg; $P < .05$). Despite the differences within the groups, there were no statistically significant differences between the groups for any outcome measure ($P > .05$). No group demonstrated improvement in pinch.[218]

V

Level V studies provide foundational justification for neutral (0°) wrist positioning of the orthosis based on carpal tunnel pressure measurement. Gelberman et al[104] (n=27) and Rojviroj et al[246] (n=49) measured carpal tunnel pressure via indwelling catheters in individuals with and without CTS with the wrist in neutral (0° wrist flexion/extension), 90° flexion, and 90° extension. Authors of both studies demonstrated the neutral wrist position was associated with the least carpal tunnel pressure and full extension was associated with the greatest pressure. Weiss et al[288] (n=24) used indwelling catheters to evaluate carpal tunnel pressure during active positioning. These authors concluded that the lowest carpal tunnel pressure in those with CTS (n=4) occurred with the wrist positioned at a mean ± standard deviation of 2°±9° flexion and 1°±9° ulnar deviation and in controls (n=20) with the wrist at 2°±9° extension and 2°±6° ulnar deviation. Kuo et al[156] (n=17) concluded neutral wrist position (0° extension) was most frequently associated with the least pressure in the carpal tunnel but that optimal position varied between individuals.

MP joint position

II

Bulut et al[48] compared the use of a prefabricated, cotton polyester wrist orthosis (0 to 5° extension) to a volar, custom-fabricated, thermoplastic wrist (0 to 5°extension) and MP joint (0 to 10° flexion) orthosis in a non-blinded trial of 33 patients (54 hands) with mild-to-moderate CTS. After 4 weeks of night use, both groups improved in all clinical, subjective, and electrophysiological outcome measures. The only statistically significant difference between groups was the CTQ-FS in favor of the custom-fabricated wrist and MP joint orthosis (MD= -.61±.52) versus the pre-fabricated wrist-only support (MD=-.06±.84; P=.012).

II

In a non-blinded trial, Golriz et al[115] compared the use of 6 weeks of wrist immobilization with either a custom-fabricated volar, neutral wrist orthosis or the same orthosis with the MP joints positioned in 0-10° of flexion in 24 individuals with mild-to-moderate CTS symptoms. Outcome measures were a pain visual analogue scale (VAS), the DASH questionnaire, and grip and lateral pinch strength. Participants wore the orthoses at night and during the day “as much as possible.” Both groups improved in all outcome measures (P≤.040) but differences between the groups were significant for pain VAS (P=.02) and the DASH questionnaire (P=.03), both favoring the wrist plus MP joint orthosis.[115]

V

Manente et al[180] measured carpal tunnel and flexor retinaculum dimensions and lumbrical insertion to flexor retinaculum distances via ultrasound imaging in individuals with mild-to-moderate CTS (n=5) and controls (n=5) with and without a prefabricated, soft hand based orthosis which immobilized the middle and ring fingers in composite extension and the MP joints of the small and index finger at 0° extension with the IP joints free to flex but restricted dorsally. Participants were positioned with their wrists in “neutral” during sonographic

measurements of the carpal tunnel. Measurements were taken at the level of the pisiform and the hook of the hamate. With the orthosis in place, the transverse diameter and total CT area increased in individuals with CTS (P<.05) as did the transverse diameter in controls while wearing the support. The same result was reported when measurements were taken at the hook of the hamate for the CTS group with the addition of a significant reduction in the flexor retinaculum thickness and increase in the distance from the proximal origin of the second lumbrical muscle to the distal edge of the tunnel (P<.05). For the controls at the level of the hook of the hamate, the only significant results were a decrease in the flexor retinaculum thickness and an increase in the lumbrical origin to flexor retinaculum distance (P<.05). The author concluded the use of the support increased carpal tunnel space and prevented lumbrical muscle incursion into the tunnel. These results should be interpreted with caution due to the small sample size, lack of blinding and opportunity for bias as the lead author was the inventor of the orthosis.[180]

V

Keir et al[148] and Rempel et al[238] noted the impact of MP joint and forearm position on carpal tunnel pressure. Keir et al[148] reported that the position of the MP joints had a significant effect on carpal tunnel pressure during passive wrist motion in all planes, with 0° MP flexion producing the highest pressures, 90° MP flexion the next highest, and 45° MP flexion the least pressure in 14 asymptomatic[238] individuals. Rempel et al[238] reported the highest carpal tunnel pressures were recorded during active forearm supination with 90° of MP joint flexion and the lowest were recorded with the forearm actively positioned in 45° pronation with 45° MP joint flexion. Participants (n=17) maintained a neutral wrist position (0° flexion/extension, 0° ulnar/radial deviation) during the trial.

Orthosis Prescription

Orthosis prescription consists of duration and length of wear.

II

Walker et al[285] compared full-time use of a custom-fabricated, thermoplastic neutral wrist orthosis with night-only use in 17 individuals (24 hands) with CTS symptoms of all severity levels. Following 6 weeks of treatment, both groups showed improvement in median DSL, CTQ-SSS, and the CTQ-FS. The full-time orthosis group also demonstrated improved DML compared to the night-only group. Adverse effects were not reported. Page et al's[222] analysis revealed MDs favoring the full time wear group (CTQ-SSS MD=-.21 95% CI -.83, .41; CTQ-FS MD=-.21 95% CI -.87, .45; DML MD=-.63 95% CI -2.05, .79; and SDL MD=.05 95% CI -.87, .45) compared to night use but concluded the bidirectional ESs and low effect estimate precision prevented identification of a benefit of full-time use over night-only use.

Orthosis versus Tendon and Nerve Gliding Exercises

II

Schmid et al[253] compared the short-term effects of a prefabricated, night wrist orthosis (unspecified wrist position) versus tendon and nerve gliding exercises (10 repetitions performed 10 times per day) on signal intensity changes and palmar ligament bowing recorded via MRI;

CTQ (combined SSS and FS) scores, pain VAS, numbness VAS, and patient-specific functional scale scores. Authors examined 20 participants at baseline, 10 minutes following the intervention (MRI changes only), and at 1 week following the intervention. Results following 1 week of treatment indicated that both groups improved in median nerve signal intensity at the carpal tunnel inlet (P=.036), combined CTQ scores (MD=-.3 for both groups; P=.001), and the patient-specific functional scale (MD=2.1 for exercise and 2.9 for the orthosis; P<.05). Numbness VAS scores did not change significantly following either treatment. Authors concluded the decrease in MRI signal intensity could represent either a decrease in edema or a decrease in blood flow.[253]

Orthosis versus Oral Steroid

II

Mishra et al[193] (n=40) compared a neutral prefabricated orthosis worn for 4 weeks at night and "as much as possible" during the day with 4 weeks of oral steroid use. Both groups improved on the CTQ-SSS and CTQ-FS at the end of 4 and 12 weeks (P<.001). Both groups improved on DSL and SNCV at 12 weeks compared to baseline (P<.03). The oral steroid group also improved on DML at 12 weeks (P=.001). The only significant differences between the 2 groups were for the CTQ-FS at 4 and 12 weeks (P<.03) and for SNCV at 4 weeks (P<.047) favoring the steroid intervention. Madjdinasab et al[177] compared 6 weeks of orthosis use (commercially available orthosis worn at night and as long as possible during the day) to 2 weeks of oral prednisolone (20 mg/day) use in 43 individuals with mild-to-moderate CTS. Outcome measures included median DSL, DML, and sensory and motor conduction velocity and were evaluated at baseline and 6 weeks. Both groups showed improvement in DSL and SNCV at 6 weeks (P=.0001). There were no statistically significant differences on any outcome measure between the 2 groups.

Orthosis versus Steroid Injection

II

So et al[265] compared the effects of a local steroid injection versus a cotton-polyester, neutral wrist orthosis after 4 weeks of treatment in 50 individuals (25 per group) with CTS (all severities). Outcome measures included the CTQ-SSS, CTQ-FS, patient satisfaction, the NHPT, duration of sick leave, pain medication use, and side effects. Both groups showed statistically significant improvement on the CTQ-SSS and CTQ-FS (P<.022), and the steroid group improved on the NHPT (P=.038). The only change score to reach clinical significance was the CTQ-SSS for the steroid group (-.67). There were differences between the 2 groups on patient satisfaction (MD between groups was equal to 2 points on 5-point numeric rating scale; P=.04) and use of pain medication (measured in days of use; raw data not provided; P=.04) favoring the injection. There were no other differences between the 2 groups at 4 weeks after treatment. Four individuals in the orthosis group reported discomfort while wearing the device and 3 individuals in the injection group reported short-lasting pain after the injection.

II

Chesterton et al[64] reported on the effects of a steroid injection (n=96) compared to 6 weeks of night-time pre-fabricated wrist orthosis use (n=96). The orthoses were positioned from "neutral

to 20º of extension." Outcomes were collected at 6 weeks and 6 months. Measures included CTQ-total score, CTQ-SSS, CTQ-FS, pain intensity, insomnia due to hand/wrist pain, referral to surgery, surgery, use of herbal remedies at 6 months, and use of over-the-counter or prescription medication use at 6 months. Authors reported significant improvement in the injection group at 6 weeks in the CTQ total score (adjusted MD=-.32 95% CI -.48, -.16; P=.0001) and similar findings in the CTQ-SSS (adjusted MD=-.35 95% CI -.53, -.17; P=.0001), CTQ-FS scales (adjusted MD=-.26 95% CI -.43, -.09; P=.0031), and pain intensity (adjusted MD=-.97 95% CI -1.64, -.30; P=.0049). However, at the 6-month follow-up, data showed that the orthosis group continued to improve on the CTQ scales and in pain intensity while the injection group did not and there were no significant differences between the 2 groups on any of the outcome variables studied. Adverse effects were reported by both groups. The steroid group adverse effects included skin changes (3%), hot flushes (15%), transient increase in wrist or hand pain (46%), and 34% reporting pain lasting > 3 days. In the night support group, 6% reported the supports were uncomfortable resulting in inconsistent use.[64]

Orthosis versus Carpal Tunnel Release

II

In a single-blinded trial, Gerritsen et al[109] compared the short and long-term effectiveness of orthoses (fabricated or off-the-shelf, worn at night and during the day as needed) and CTR surgery in 147 individuals with mild-to-moderate idiopathic CTS. Participants were randomly assigned to use the orthosis for 6 weeks or to undergo surgery (open CTR). Participants were assessed at 1, 3, 6, 12, and 18 months (84% retention) post randomization. Primary outcome measures were subjective report of improvement, number of nights of symptom-disturbed sleep, and the severity of the patient-determined "most important symptom" (ranked on an 11-point scale). Secondary measures included CTQ scales and electrodiagnostic studies. Treatment success was defined as completely recovered or much improved on a patient-reported 6-point scale ranked from "completely recovered" to "much worse". At 1 month the orthosis group showed greater success (42% versus 29% for the surgery group), but at all other time points, more participants in the surgery group reported greater success. After 3 months, 80% of the surgery group were determined to be successfully treated compared to 54% of the orthosis group, and at 18 months the success rate was 90% for the surgery group versus 75% for the orthosis group. Data from participants were analyzed as assigned in their original groups and by 18 months, 41% of those in the orthosis group had undergone surgery. In the surgery group, 67% of patients reported adverse effects compared to 52% of the orthosis group. These effects included complex regional pain syndrome, pillar pain, swelling, discomfort from the orthosis, wound complications, skin irritation, wrist stiffness, and painful or hypertrophic scars. Because these were reported in the original assigned groups, comparison of the rates of adverse effects between interventions could not be made.

II

In a non-blinded, randomized trial, Ucan et al[278] studied 57 participants with mild-to-moderate CTS divided into 3 groups: neutrally-positioned, prefabricated wrist orthosis worn at night and during the day "whenever possible" (n=23), a local steroid injection and orthosis (n=23), or open CTR surgery (n=11). Non-surgically-managed participants wore the orthoses for 3 months. Outcomes were evaluated using the NCS results and CTQ scales at 3 and 6 months. At 3 months,

all 3 groups demonstrated statistically significant improvements in median DML, CMAP, SNCV and CTQ scales (P<.006). For the CTQ-SSS, the CTR group score was higher (indicating greater symptoms) than the other 2 groups (P ≤.011), and for the CTQ-FS, the orthosis and CTR group demonstrated higher scores (indicating more difficulty with function) than the injection and orthosis group (P=.001) At 6 months, all groups remained statistically improved in DML, CMAP, SNCV, and CTQ scales. For the CTQ scales, the CTR group scores continued to improve compared to the other groups (CTQ-FS: P=.03; CTQ-SSS: P=.004) while the other 2 groups' scores worsened. Complications were reported for 2 of the participants in the CTR surgery group: one with scar tenderness which resolved and one developed complex regional pain syndrome.[278]

Orthosis Combined with Patient Instruction

II

Hall et al[125] concluded CTS management consisting of a full-time, neutrally-positioned wrist orthosis plus patient instruction was more effective than no intervention. In this randomized, single-blinded trial, 30 patients with all severity levels of CTS wore 1of 3 commercially-available supports or a custom-fabricated wrist orthosis for 8 weeks and attended 2 sessions of patient instruction (pathology, risk identification, symptom self-management, and postures/activities that aggravate symptoms including sleeping postures and repetitive wrist and hand movements). The 24 participants in the control-group received no intervention. At the end of the treatment period, the orthosis group showed statistically significant improvements in the CTQ (CTQ-SSS MD=-.42 vs. control MD=.03 P<.001; CTQ-FS MD=-.20 vs. control MD=.08; P=.015) and pain VAS (MD=-1.58 vs control MD=.65 P=.001). Improvement was significant for grip strength, but the control group demonstrated greater grip improvement (MD 1.85 kg vs 1.07 kg; P=.02) than the intervention group. No significant changes were demonstrated for Phalen's test, PPB test, or SWMT for either group.[125]

Orthosis Combined with Steroid Injection

II

Wang et al[286] studied the effect of an ultrasound-guided steroid injection into the carpal tunnel combined with orthosis use compared to the injection alone in 52 individuals with mild or moderate CTS. Participants in the experimental group wore a volar, custom-fabricated neutral wrist orthosis during sleep and as much as possible during the day for 12 weeks following injection. Outcome measures included CTQ scores, pain VAS, and NCS results, and they were evaluated at baseline and 6 and 12 weeks. Both groups showed significant improvement in CTQ scores, VAS, DML, SNCV, and SNAP at 6 and 12 weeks (P<.001). There were no differences between the groups at 6 or 12 weeks. At 12 weeks, the response to treatment diminished in the injection-alone group (CTQ-SSS increased which suggests worsening symptoms from 1.28 to 1.49 between 6 and 12 weeks), while the effects of treatment in the combined group remained. There were statistical differences in change scores between groups at 12 weeks in the CTQ-SSS (MD=.48 95% CI .09, .88; P=.032), CTQ-FS (MD=.37 95% CI .06, .67; P=.019), SNCV (MD=3.38 95% CI .54, 6.22; P=.015), and SNAP (MD=3.21 95% CI 0, 6.46; P=.025) favoring the combined treatment. The authors concluded the combined treatment had sustained effects on sensation, function, and NCS that were not present in the injection only group.[286]

IV

Courts[76] evaluated grip, pinch, and symptom reduction following the use of a wrist orthosis positioned in 10 to 15° extension in women who developed CTS during pregnancy (n=82). The orthoses were worn at night and during the day. After 1 week, grip and pinch strength improved and symptoms were reduced. Of the 58% participants who returned postpartum, 76% reported complete resolution of symptoms. Ekman-Ordeberg et al[87] reported 82% of 56 pregnant women with carpal tunnel symptoms improved after wearing a night wrist orthosis for 2 weeks and 93% were resolved post-partum.

Evidence Synthesis and Clinical Rationale

The use of an orthosis for treatment of CTS is widely accepted despite the lack of high-quality studies. There are limited data supporting orthosis use over no intervention to improve symptoms and function in the short term for individuals with mild or moderate severity CTS. The most frequently studied orthoses were commercially-available wrist orthoses (multiple manufacturers and designs) and custom-fabricated volar or ulnar orthoses immobilizing the wrist or adding the MP and IP joints in a variety of positions. Some studies used a variety of wrist supports within the same experimental group. Evidence from basic science studies supports positioning the wrist near neutral in both the sagittal and frontal planes, although individual variation has been demonstrated. Including the MP joints has shown positive effects in clinical and bench studies, although the evidence on the desired angle is conflicting (0 to 10˚ versus 45˚) and MP joint inclusion further limits functional use during wear.

There are conflicting results comparing an orthosis to oral steroid use in the short term, however when an orthosis was compared to steroid injection, results favored the injection in the short term[64, 265] but effects of the 2 treatments when implemented separatley were equal at 6 months post treatment.[64] Repeating this study with the wrists immobilized in 0° extension might produce a different result. When an orthosis was combined with a steroid injection, the effects were superior to the injection alone.[278, 286] Adverse reactions for the steroid injection include thinning skin, pigment changes, hot flushes, and increased pain.[64]

When comparing an orthosis to surgery, the orthosis demonstrated improvement over surgery in the short term but long-term results favored surgery.[110, 278] Surgery is associated with increased cost and may have a higher rate of complication as reported in these studies. Reported surgical risks included pillar pain, wound complications, swelling, and hypertrophic or painful scars. Reported orthosis risks included difficulty falling asleep, temporary paresthesia upon removal, stiffness, skin irritation, discomfort, and swelling. An additional risk is skin breakdown, especially when sensation is impaired and the orthosis does not fit properly. The availability of prefabricated orthoses and the lower cost make this a convenient intervention, however, the angle of wrist immobilization varies among manufacturers and should be checked and adjusted by a practitioner to find the most comfortable angle for the patient. The use of a neutral-positioned orthosis may reduce symptoms for individuals considering or waiting for surgery. There is evidence to support orthosis use in the short-term for relieving symptoms and improving strength in women who develop CTS during pregnancy.

Gaps in knowledge

There is no consensus on the most appropriate orthosis material, design, prescription, or position or evidence to accurately identify ideal candidates for orthosis intervention. Many studies lacked a control group, an adequate sample size, adequate randomization, and/or blinding. Most studies lacked participant compliance data for orthosis use as well as use of meaningful, validated outcome measures. Many studies were confounded by the use of multiple interventions masking the effect of any single intervention. Identification of the most effective orthosis characteristics should be determined prior to investigating combining non-surgical interventions. The majority of studies enrolled patients with mild-to-moderate CTS and no conclusion can be drawn with respect to the effects of orthoses on those with severe CTS. Demonstrated differences in ideal positioning could be explored through the development of a non-invasive tool for measuring carpal tunnel pressure; providing guidance regarding individual wrist and MP joint positioning.

Recommendations

B

Clinicians should use a neutrally-positioned wrist orthosis worn at night for short-term symptom relief and functional improvement for those individuals with carpal tunnel syndrome seeking non-surgical management. Effectiveness may be improved if combined with a steroid injection or patient education on pathology, risk identification, symptom self-management, and postures/activities that aggravate symptoms.

C

Clinicians may suggest adjusting wear time to include daytime, symptomatic, or full-time use when night-only use is ineffective at controlling symptoms in individuals with mild-to-moderate carpal tunnel syndrome. Clinicians may also add metacarpophalangeal joint immobilization or modify the wrist joint position for individuals with carpal tunnel syndrome who fail to experience relief.

C

Clinicians should recommend an orthosis for women experiencing carpal tunnel syndrome during pregnancy and should provide a postpartum follow-up evaluation to examine the resolution of symptoms.

BIOPHYSICAL AGENTS

Thermotherapy
Dry Heat

II

In a randomized, single-blinded trial, Michlovitz et al[192] compared the effect of a disposable wrist low-level heat wrap to an oral placebo in 24 individuals diagnosed with CTS (all severities). The heat wrap was worn for 8 hours per day while the control group took an oral placebo 4 times per day. Both groups were treated for 3 days and followed for an additional 2 days. After 3 days, the heat wrap group demonstrated improved scores relative to the

placebo group including reduced pain (MD=-2.18 versus -.95; P=.001); reduced joint stiffness (MD=-21.8 versus -4.9; P=.004); increased grip strength (MD=6.6 versus -0.3; P=.003); self-reported disability scores (MD=-27.1 versus - 2.67; P=.0015); CTQ-SSS (MD=-.90 versus -.20; P=.001) and CTQ-FS (MD=-.65 versus.00; P=.006). While the symptom improvements for both groups persisted to day 5, improvement in CTQ-FS scores did not. Adverse effects were reported and for the heat wrap included coldness in the fingers and for the oral placebo, dyspepsia.[192]

Paraffin

II

Chang et al[58] compared the use of paraffin (dip-and-wrap applied for 20 minutes) to pulsed, direct-contact US (1 MHz, 1.0 W/cm^2, 1:4 duty cycle, 5 cm^2 sound head, 5 minutes) given twice per week for 8 weeks in 47 patients with CTS (all severities). Participants in both groups wore a custom-fabricated neutral wrist orthosis at night for 8 weeks. Outcome measures included the CTQ-SSS and FS, pain scale, sensory threshold, palmar pinch strength, DML, and DSL. After 8 weeks, both groups improved on the CTQ-SSS (ES for both groups was equal to .63) and sensory threshold (P<.03). The US group demonstrated significant improvement in CTQ-FS, pain scale, and palmar pinch following treatment when compared to baseline; however, the only significant difference between the paraffin and US groups was the CTQ-FS score favoring US (MD=-0.3 compared to paraffin MD=0.1, P=.04, ES=.38). A limitation of this study was that there was no control group. No adverse effects were reported.[58]

Microwave and Short Wave Diathermy

II

Frasca et al[100] compared the effectiveness of microwave diathermy to sham diathermy in patients with idiopathic mild-to-moderate CTS. In this double-blind trial, 22 patients (34 hands) were randomized to receive active or sham microwave diathermy for 20-minute sessions, twice weekly for 3 weeks. Outcome measures included pain VAS, CTQ-SSS, CTQ-FS, and NCS (DML and sensory NCV). At the end of 3 weeks, the active treatment group demonstrated statistically significant improvement in pain severity (MD=-2.0; P=.002), CTQ-SSS (MD=-.54; P=.0001), and CTQ-FS (MD=-.50; P=.002). There were significant differences between the active and sham treatment groups in pain severity (P=.004) and CTQ-SSS (P=.009) but not in the CTQ-FS. There were no significant differences for either group in electrophysiology parameters studied. There were no reported adverse effects.[100]

II

Incebiyik et al[136] compared the effectiveness of short wave diathermy combined with a hot pack and nerve and tendon gliding exercises to sham short wave diathermy in 28 patients (52 wrists) with mild-to-moderate severity CTS. Participants received a hot pack application for 15 minutes followed by sham or active short wave diathermy for 15 minutes, followed by 3 sets of 10 repetitions of nerve and tendon gliding exercises. Treatments were given 5 times per week for 3 weeks. Outcome variables included the Tinel sign, Phalen test, reverse Phalen test, carpal

compression test, pain VAS, CTQ-SSS, and the CTQ-FS. At the end of 3 weeks, improvement in all outcome variables for the active treatment group were statistically better than the sham group (P<.003). The MDs between the 2 groups for pain, CTQ-SSS, and CTQ-FS were 1.88, 9.09, and 8.37. There was no significant improvement in any outcome measure for the sham group. Adverse effects were not provided.[136]

Evidence Synthesis and Clinical Rationale

Studies have shown positive, short-term effects of using superficial heat in individuals with CTS. Heat wraps, paraffin, and short-wave and microwave diathermy have shown positive effects in the short term. When combined with an orthosis, the use of paraffin however was not superior to pulsed US.[58] Individuals with CTS should be instructed in the risks of applying thermal agents to sensory-impaired tissue and should be advised to perform frequent skin checks. Heat should not be used in the presence of inflammation.

Diathermy is contraindicated in areas where sensation is severely impaired and over areas with metal implants. It should not be performed on a patient who is pregnant or be performed by a pregnant operator.[37] Other forms of superficial heat (wrist heat wrap) have shown similar results and can be done without concerns for pregnancy, metal implants, or need for clinic visits and can be delivered at lower expense.

Recommendations

C

Clinicians may recommend a trial of superficial heat for short-term symptom relief for individuals with carpal tunnel syndrome.

C

Clinicians may recommend the application of microwave or short-wave diathermy for short-term pain and symptom relief for patients with mild-to-moderate idiopathic carpal tunnel syndrome.

Electrical Stimulation

Interferential current

II

Koca et al[150] randomly allocated 63 individuals with mild-to-moderate CTS to a pre-fabricated, night-wear wrist orthosis group (wrist positioned in 0 to 15°extension), a transcutaneous electrical nerve stimulation (TENS) group (100 Hz; 80 ms pulse duration) with electrodes placed on the transverse carpal ligament and the palm, or an interferential current (IFC) group (base frequency: 4000 Hz; modulation frequency range: 20 Hz, Δ*F* of 10 Hz; slope of 1/1) using a quadrupolar electrode placement with 2 electrodes on the mid portion of the volar forearm, 1 on the palm, and 1 on the thenar eminence area. Electrical modalities were administered for 20 minutes, 5 times per week for 3 weeks. Outcomes were measured by pain VAS, CTQ-SSS, CTQ-FS, and NCS. At 3 weeks post treatment, all groups improved significantly on VAS, CTQ-SSS, CTQ-FS, and median SNCV but not on DML. There were no statistically significant

differences between the orthosis and TENS groups. The IFC group was significantly better than the other groups for change in pain VAS (MD=-3.45 vs orthosis group MD=-1.94 and TENS group MD=-1.38; P<.001) SNCV (MD=1.6 vs orthosis group MD=0.82 and TENS group MD=1.72; P<.05). The IFC group demonstrated significant improvement over the TENS group for CTQ-SSS (MD=-1.2 compared to TENS MD=-.69; P<.05) and CTQ-FS (MD=-.90 vs TENS MD=-.43; P<.05), but there was no difference compared to the orthosis scores. In this study, IFC demonstrated greater pain change and SNCV scores than the orthosis or TENS, however, the small sample size and lack of a control group weaken the result. The frequency of IFC treatment (5 days per week) and additional cost may not be justified in light of other non-surgical interventions. Interferential current should not be used in patients with a pacemaker.[37]

C

Clinicians may offer a trial of interferential current for short-term pain symptom relief in adults with idiopathic, mild-to-moderate carpal tunnel syndrome.

Light Agents

II

Low-level laser therapy (LLLT) is a form of electromagnetic energy that is monochromatic (single wavelength) and coherent (in phase).[53] In a recent, high-quality Cochrane Review, Rankin et al[237] reviewed 22 RCTs on LLLT for treatment of CTS published through December 2016. Trials compared LLLT to placebo and other non-surgical interventions. Authors concluded there was insufficient evidence of a clinical effect of LLLT in the non-surgical management of CTS. They also concluded there was insufficient evidence to support long-term benefits of LLLT versus placebo or US.[237]

II

Raeissadat et al[235] used Bioptron® light therapy, a form of non-laser, low-energy light therapy (polychromatic, incoherent) with wavelengths ranging from 480-3400 nm in 44 adult patients with mild or moderate CTS in a non-blinded, randomized clinical trial. The experimental group received 12, 8-minute light treatments over a 4-week period and wore a neutral wrist orthosis full time except for hygiene. The control group also wore the orthosis but did not receive the light therapy. Outcome measures included pain VAS and electrophysiological parameters. At 8 weeks, both groups demonstrated improvement in pain VAS (control MD=-2.28; P<.05 and light therapy MD=-2.42; P<.05) and median DSL (control MD=.23 ms; P<.05 and light therapy MD=.18 ms; P<.05), but there were no statistical differences between the 2 groups on any measure (P>.05). There were no adverse effects.[235]

IV

Stasinopoulos et al[269] also applied Bioptron® light therapy for 6 minutes 3 times per week for 4 weeks in patients with idiopathic mild-to-moderate CTS (n=25) and provided outcome data using descriptive statistics. At 4 weeks, 92% reported improvement in nocturnal pain and 84% reported improvement in paresthesia. At the 6-month follow-up 100% reported improvement in night pain and 36% were pain free. Paresthesia improved in 92% of participants and 28% had complete

resolution. The results of this study are inconclusive due the lack of blinding, not using validated outcome measures, a small sample size, and lack of a control group.[269]

Evidence Synthesis and Clinical Rationale
There is no evidence of a biological effect of LLLT or light therapy on CTS. There is a lack of consensus regarding the optimal wavelength, dosage, frequency, and duration of treatment. Side effects of LLLT, including pain and tingling that subsided after the treatment, have been reported;[241] however, Rankin et al[263] concluded there is insufficient evidence on adverse events.

Recommendation

B

Clinicians should not use low-level laser therapy or other types of non-laser light therapy for individuals with carpal tunnel syndrome.

Sound Agents

Ultrasound

II

Oztas et al[219] compared 2 different continuous US intensities to sham US in 18 female participants (30 hands; 10 per group) with mild-to-moderate idiopathic CTS of more than 6 months duration. Groups were treated with 3MHz US applied for 5 minutes at either 1.5 W/cm^2, 0.8 W/cm^2, or 0.0 W/cm^2 (sham), 5 times per week for 2 weeks. Outcomes were measured 5 days after the last session and included pain VAS, night or day pain or paresthesia (4-point scale), frequency of night waking (4-point scale), and NCS. All groups improved significantly in all outcome measures (P<.05) except NCS (P>.05). There were no statistically significant differences between the 3 groups on any outcome measure.[219]

II

Armagan et al[17] compared pulsed (1:4) and continuous US (1.0 MHz, 1.0 W/cm^2) to sham US (0.0 W/cm^2) in 46 females with mild-to-moderate idiopathic CTS in a prospective, randomized, double-blinded study. The length of each treatment session was not reported but the frequency and duration was 5 times per week for 3 weeks. All participants also wore a custom-fabricated orthosis (night and day) during the treatment period. Outcome measures included CTQ-SSS, CTQ-FS, pain VAS, and NCS. At the end of 3 weeks, there was significant improvement in all groups in the CTQ scales (P<.05) and VAS (P<.01), but there were no significant differences between groups (P>.08). For DSL and SNCV, there were small, but statistically significant improvements in the pulsed US and sham groups from baseline (P<.05) but no differences between the groups for any NCS values (P>.09).[17] Due to the lack of a true control group, the difference could have been due to the orthosis or the natural course of the disease.

II

In a randomized double-blinded trial, Ebenbichler et al[86] compared sham US to pulsed US (25% duty cycle; 1 MHz; 1.0 W/cm^2) applied for 15 minutes in 34 adults with bilateral, mild-to-

moderate idiopathic CTS (duration greater than 6 months). Participants were treated for 7 weeks (5 times per week for 2 weeks and twice weekly for 5 weeks) for a total of 20 sessions. Outcome measures included change scores in subjective complaint (pain and paresthesia) VAS, worst complaint VAS, sensory loss VAS, grip and pinch strength, NCS (DML and SNCV), and overall improvement (5-point scale). Changes in scores were evaluated between baseline and 2 weeks, 7 weeks (end of treatment), and 6 months post treatment. Subjective measures favored the active treatment at each time point (P<.05) except for worst pain at 2 weeks (P=.125). Grip strength was better in the active treatment group at 7 weeks (active treatment MD = 3.87 kg versus sham MD=-.09 kg; P<.0005) and 6 months (active treatment MD = 5.44 kg versus sham MD=-1.99 kg; P<.0005). Pinch strength was better in the treatment group compared to the control group at 6 months (active treatment MD=.49 kg versus sham MD=-.22 kg; P=.014). All nerve conduction study data favored the active treatment group at each time point (P<.001). Good or excellent results were reported by 76% of individuals in the active treatment group compared to 32% of individuals in the sham group.[86] No adverse effects of US treatment were reported.

II

In a randomized, single-blinded trial of 46 wrists with bilateral mild-to-moderate CTS**,** Baysal et al[35] compared 3 groups: 1) pulsed US plus an orthosis; 2) tendon and nerve gliding plus an orthosis; and 3) pulsed US plus tendon and nerve gliding plus an orthosis. All orthoses were custom-fabricated (volar, neutral position, worn day and night for 3 weeks) and US treatments were provided using 1:4 duty cycle, 1.0 MHz at 1.0 W/cm^2 for 15 minutes. The US was delivered 5 times per week for 3 weeks. Outcomes were assessed at the end of treatment and at an 8-week follow-up and included pain VAS, presence of a positive Tinel sign and Phalen test, grip and pinch strength, 2PD, CTQ-SSS, CTQ-FS, DSL, DML, and patient satisfaction. All groups improved in all measures at the 3 and 8-week follow-ups (P<.05) except 2PD and DML (no group improved; P>.05), and DSL (only the US-orthosis and US-exercise-orthosis groups improved [P<.05]). For patient satisfaction, 25% of the exercise-orthosis group reported excellent/good satisfaction and 61% of the exercise-US-orthosis group reported excellent/good satisfaction. There were no significant differences between groups on any outcome variable.[35] The improvement cannot be attributed to a single intervention or to the combination of interventions due to the lack of a control group.

Evidence Synthesis and Clinical Rationale

Based on the results of 2 level II studies, thermal US has not been shown to be better than sham US.[17, 219] Evidence on pulsed US is conflicting. One study found positive benefits, but authors reported a priori differences between groups in subjective complaints and grip strength (active US treatment being worse) that may suggest greater severity in this group.[86] Also, based on findings from studies where US was combined with other treatments, there is conflicting evidence on the benefit of adding non-thermal US to treatment regimens that include an orthosis and/or tendon and nerve gliding exercises.[17, 35, 58] Last, there is insufficient evidence to support 1.5 W/cm^2 versus 0.8 W/cm^{2,} and there is insufficient evidence to support 1 MHz versus 3 MHz.[219] Given the additional treatment expense and time commitment, there is not enough evidence for or against the use of non-thermal ultrasound in patients with mild-to-moderate CTS.

Gaps in knowledge

High-quality, controlled studies on the effects of both thermal and pulsed US in individuals with CTS are needed.

Recommendations

C

Clinicians should not use thermal ultrasound in the treatment of patients with mild-to-moderate carpal tunnel syndrome.

D

There is conflicting evidence on the use of non-thermal ultrasound in the treatment of patients with mild-to-moderate carpal tunnel syndrome, and therefore no recommendation can be made.

Transdermal drug delivery

The use of topical anti-inflammatory drugs, both steroid and non-steroid has been investigated for treatment of carpal tunnel syndrome based on the inflammatory model of pathology. Localized inflammation has been suggested to contribute to the pathology of CTS in 1 of 4 ways: by decreasing the space in the tunnel due to the presence of inflammatory infiltrates, decreasing the circulation within the median nerve due to intraneural infiltrates, fibrosis of the nerve due to inflammatory infiltrates, or increasing the work of the flexor tendons gliding through resistance produced by inflammatory infiltrates.

Phonophoresis

II

In a double-blinded trial, Yildiz et al[302] randomized 51 adults (76 hands) with idiopathic mild-to-moderate CTS to 1 of 3 groups: sham US, active pulsed US, or 2.5% ketoprofen gel phonophoresis. Forty-four individuals (68 wrists) completed the protocol but intention-to treat analysis was performed using all participants who were initially randomized. Ultrasound parameters for the active treatment groups were: 1 MHz frequency, 1.0 W/cm^2, and 25% duty cycle. Participants were treated for 15 minutes, 5 times per week for 2 weeks. Participants also wore custom-fabricated volar wrist orthoses (0 to 5° wrist extension) full time for 8 weeks. Outcomes were measured at 2 and 8 weeks and included CTQ scales, pain VAS, and NCS. All groups improved in all measures; however, the phonophoresis group improvement for the pain VAS (MD=-5.06) was statistically greater than the other 2 groups (sham US MD=-2.48; P =.002; pulsed US MD=-2.19; P =.004). There were no other statistically significant differences between the 3 groups.[302] Authors reported there were no complications from the interventions.

II

Soyupek et al[267] compared 4 different interventions for mild-to-moderate CTS. In this single-blinded (assessors) trial, 51 patients (84 hands) were assigned to 1 of 4 groups: local steroid injection (LSI group); corticosteroid (0.1% betamethasone valerate cream) phonophoresis (PCS group), NSAID (diclofenac diethylammonium gel) phonophoresis (PNS group), or a volar, neutral wrist orthosis. Phonophoresis was applied at 3 MHz, 1.5 W/cm^2 for 10 minutes, 5 days per week for 3 weeks using a 5 cm^2 sound head. The orthoses were worn full time for 15 days, and only when symptomatic for the remaining 6 days. Outcome data were collected at baseline

and 3 months following treatment. There were significant baseline differences for some outcome measures between the groups (Duruöz Hand Index (DHI), SNCV, SNAP, DSL) but no baseline differences for grip strength, hand dexterity, sensory threshold (SWMT), Phalen sign, Tinel test, VAS. The only statistically significant difference between groups was for Tinel sign favoring PCS group (P=.04). Pre and post-treatment differences for the PCS group were significant for Tinel's (P≤.003), grip (P≤ 0.003), SWMT of the middle finger (P=.046) and NCS (SNCV, MDL, SDL) (P≤ .049). The PNS group demonstrated improvement in pain VAS, grip and dexterity (P≤.003) The orthosis group demonstrated improved pain VAS (P=.00) and SDL (P=.002), and the LSI group improved in the DHI and pain VAS (P≤.006). Authors concluded the greatest improvements were observed with the PCS group in strength, function, SNCV, DSL, and DML and with the PNS group for pain.[267]

II

In another study, Soyupek et al[268] compared phonophoresis with corticosteroid (PCS), phonophoresis with NSAID (PNS) (medications listed above), and volar neutral wrist orthoses in patients with mild-to-moderate CTS. In this trial, 47 patients (74 hands) were randomized into 1 of the 3 groups. Phonophoresis was applied at 3 MHz, 1.5 W/cm^2 for 10 minutes, 5 days per week for 3 weeks using a 5cm^2 sound head. After 3 months, all groups improved in all clinical measures. The PCS group scores improved for VAS (MD=-30, P<.017), CTQ (MD=-1.5, P<.017), percentage of participants with positive Phalen test (MD=-32.1%, P<.017), Tinel sign (MD=-39.3%, P<.017), and nerve dimensions as measured by US imaging (anterior-posterior MD=-.24, cross-sectional area MD=-.03, P<.017) (unit of measure not reported). The PNS group scores improved in VAS (MD=-23.48, P<.017), CTQ (MD=-1.18, P<.017) and percentage of subjects with positive Phalen sign (MD=-32.9%, P<.017). The orthosis group scores improved in CTQ-SSS (MD=-1.54, P<.017). No group improved in nerve conduction measures (P>.017). [268]

Iontophoresis

II

Amirjani et al[14] performed a randomized, double-blinded study of ~~20~~ 17 individuals with mild-to-moderate CTS comparing iontophoresis with 0.4% dexamethasone sodium phosphate to distilled water iontophoresis. The treatment was administered every other day for 2 weeks for a total of 6 treatments at a rate of 2mA-min for a total treatment dosage of 80mA-min. Participants were followed monthly for 6 months after treatment. Outcome measures included CTQ total score (SSS+FS), sensory threshold (measured using the SWMT), and NCS. At 6 months post treatment, both groups improved in CTQ scores (distilled water iontophoresis median difference=-2.0; P=.028; steroid iontophoresis median difference=-12; P<.05) but the difference between the groups was not significant (P=.25). There were no significant improvements for either group in sensory threshold (P≥.1) or nerve conduction (P≥.1). One participant reported skin erythema under the electrode which resolved in a few hours.[14]

II

Gökoglu et al[113] compared a single 40 mg methyl prednisone acetate injection with 3 sessions of iontophoresis (0.4% dexamethasone sodium phosphate) in 30 individuals (48 hands) with mild-to-moderate CTS. The iontophoresis was applied every other day for 20 minutes for a total

dosage of 40 to 45mA-min. Outcomes were measured at 2 and 8 weeks and included CTQ-SSS, CTQ-FS, and pain VAS. Both groups improved on all outcome measures however, the injection group showed greater improvements at both 2 and 8 weeks. For the CTQ-SSS, MDs at 2 and 8 weeks for the injection group were -0.8 and -1.1, respectively, and -0.6 and -0.9, respectively, for iontophoresis group (P<.05). For the CTQ-FS at 2 and 8 weeks, MDs for the injection group were -0.8 and -1.1, respectively, and for iontophoresis group were -0.2 and -0.4, respectively (P< .05). For pain VAS, the injection group at 2 and 8 weeks showed MDs=-1.7 and –4.4, respectively, compared to the iontophoresis group MDs=-2.1 and -3.7, respectively (P<.001).[113] There were no side effects for either treatment.

Phonophoresis versus Iontophoresis

II

In a single-blind study, Bakhtiary et al[31] compared phonophoresis and iontophoresis in 34 individuals (52 hands) diagnosed with mild-to-moderate CTS who were randomized into 1 of 2 groups. Each group was treated 5 times weekly for 2 weeks with 0.4% dexamethasone sodium phosphate. Phonophoresis was applied at a frequency of 1 MHz, 1.0 W/cm^2 intensity, and 25% duty cycle for 5 minutes. Iontophoresis was applied with the steroid under the negative electrode at 2 mA/min for 20 minutes (total dose=40 mA-min). Outcome measures included pain VAS, motor and sensory nerve latencies, action potential amplitudes, pinch strength, and grip strength. At 2 weeks, both groups improved in all parameters but changes in the phonophoresis group were significantly larger than those in the iontophoresis group (pain VAS MD=2.1 95% CI 1.3, 2.9, P=.001; grip strength MD=27.1N 95% CI 13.5, 40.5, P=.006; pinch strength MD=31.6N 95% CI 15.9, 47.3, P=.0002; DML MD=0.8 95% CI 0.5, 1.1, P=.0008; CMAP MD=4.1 95% CI 3.0, 5.2, P=.0001; thumb DSL MD=8.8 95% CI 5.6, 12.1, P=.004; index DSL MD=.8 95% CI 0.5, 1.1, P=.0001). At 4 weeks, both groups demonstrated regression in all outcome measures except pain VAS in the iontophoresis group and DML and DSL in the phonophoresis group. Despite the declines, the phonophoresis improvements remained significant for all outcome measures (P≤.032).[31]

II

In a non-blinded study, Gurcay et al[121] compared phonophoresis (0.1% betamethasone; 1 MHz, 1.0 W/cm^2, 10 minutes 3 times per week for 3 weeks, continuous mode) to iontophoresis (0.1% betamethasone; 2 mA for 10 minutes; 3 days per weeks for 3 weeks) to a control group in individuals with mild-to-moderate CTS. All participants (n=52) wore a night-time, volar wrist orthosis for 3 weeks (custom; thermoplastic; neutral position). Outcome measures, including the CTQ-SSS, grip strength, and dexterity measured by the nine-hole peg test, were assessed at baseline and 3 months after treatment. Results were reported in bar graph and narrative form and no baseline or outcome scores were provided. The CTQ-SSS scores improved in all groups (P≤.001). There was a statistically significant difference between the change scores in the phonophoresis and control groups in favor of the phonophoresis (P=.012). There were no other significant differences between the groups.[121] There was no report of adverse effects of the interventions.

II

In another non-blinded study, Karaty et al[142] compared a single 4 mg injection of dexamethasone plus local anesthetic to 3 weeks (15 sessions) of iontophoresis (0.4% dexamethasone sodium phosphate, 1-4mA current) or phonophoresis (0.1% dexamethasone sodium phosphate delivered at 1 MHz, 1.0 w/cm^2, 25% duty cycle) in patients with CTS. Forty-five individuals (90 hands) with early, mild, bilateral CTS were randomly assigned to 1 of the 3 groups. Outcome measures (night pain VAS, CTQ-SSS, CTQ-FS, DML, and DSL) were measured at 1 and 6 months after the start of the study. At 1 month, there were significant improvements in clinical and electrophysiological parameters for the injection and phonophoresis groups (P<.001). In the iontophoresis group, there were significant changes for the clinical parameters only (P<.001). At 6 months, the injection group outcomes remained significantly improved on all parameters (P<.01), the phonophoresis group remained significantly improved in clinical parameters only (P<.001), and the iontophoresis group did not demonstrate significant improvement over baseline for any parameter. The injection group outcomes were significantly better than the iontophoresis group for night pain at 6 months (P=.020), CTQ-SSS at 1 (P=.031) and 6 months (P=.003), CTQ-FS at 6 months (P=.011) and DSL at 1 month (P=.036). The injection group outcomes were better than the phonophoresis group for night pain at 6 months (P=.022) and CTQ-SSS at 6 months (P=.030). Authors concluded that injection or steroid phonophoresis could be used in the management of CTS[142]. Authors did not report between-group differences for iontophoresis versus phonophoresis.

Evidence Synthesis and Clinical Rationale

While there is evidence that iontophoresis with 0.4% dexamethasone sodium phosphate resulted in a positive effect on subjective outcomes, distilled water iontophoresis produced similar results, suggesting the active agent could be the electrical stimulation. Steroid and non-steroid phonophoresis demonstrated positive effects in the short term for individuals with mild or moderate severity CTS. There is evidence demonstrating improvement for short term pain relief, clinical signs, weakness, functional deficits, sensory deficits and nerve cross sectional area.[121, 267, 268, 302] Changes in NCS were conflicting.[142, 267, 268] No study included a control group, and the magnitude of improvement due to the treatment compared to the natural course of CTS could not be determined. Two of the 3 studies combined phonophoresis or iontophoresis with an orthosis masking the magnitude of the effect of the drug administration alone. For patients considering the use of anti-inflammatory medications, a local steroid injection combined with a neutral wrist orthosis may be more cost effective and efficient.

Gaps in Knowledge

To determine the efficacy of transdermal drug administration, evidence for the role of inflammation in CTS should be determined. The iontophoresis studies used dexamethasone sodium phosphate or diphosphate while the phonophoresis studies used a variety of steroid and non-steroid active drugs. No evidence was presented for the choice of drug or concentration or for treatment variables including dosage, frequency, and treatment duration. Well-designed trials with control groups and appropriate outcome measures are needed.

Recommendations

B

Clinicians should not use iontophoresis in the management of mild-to-moderate carpal tunnel syndrome.

C

Clinicians may perform phonophoresis in the non-surgical management of patients with mild-to-moderate carpal tunnel syndrome for the treatment of clinical signs and symptoms but should consider other interventions.

Athermal Agents

Magnet Therapy

II

There were 2 studies comparing the effects of magnet therapy with a placebo in individuals with CTS. In a double-blinded trial, Carter et al[55] studied 30 individuals with CTS (all severities) who wore a 1000 gauss magnet or placebo magnet strapped to their wrist for 45 minutes. Outcomes were measured at 15-minute intervals during treatment and 2 weeks post treatment. At the end of treatment, both groups reported significant pain reduction (MD for both groups=-2.4) as measured by an 11-point VAS with no statistical difference in improvement between groups. At 2 weeks post treatment, mean pain was identical for both (4.3/10) and remained below baseline levels. In a randomized, controlled, double-blinded study of 60 individuals with CTS of all severity levels, Colbert et al[72] compared 2 static magnetic field strengths (15 and 45 mT) with a sham magnet applied over the carpal tunnel nightly for 6 weeks. At 6 and 18 weeks, all groups demonstrated statistically significant improvements in CTQ scales but there were no differences between the groups (P≥.463). Adverse effects included pain under the 45mT magnet (n=1) which resolved in 2 days and skin rash under the adhesive (n=2) used to secure the magnets which also resolved with topical ointment.

Recommendation

B

Clinicians should not use or recommend the use of magnets in the intervention for individuals with carpal tunnel syndrome.

MANUAL THERAPY TECHNIQUES

II

A variety of different exercise and manual therapy interventions have been studied as potential non-surgical treatment for CTS. A Cochrane review was published in 2012 based on 16 Level II studies evaluating the effects of exercise and mobilization interventions for CTS.[223] Interventions included were carpal bone mobilization, yoga, tendon and nerve gliding exercises, neurodynamic mobilization, instrument-assisted soft tissue massage, and standard soft-tissue massage. Exercise and manual interventions were delivered as components of single or multi-intervention treatments and compared to one or more other non-surgical interventions such as orthotic devices, steroid injections, or other physical agents. Authors consistently found bias, lack of blinding, small between group differences, and CIs including effects in both directions. The use of multiple interventions precluded identifying the effect of a specific intervention. Authors

concluded there was limited and very low-quality evidence of any benefit for exercise and mobilization interventions for CTS compared to use of orthoses.[223]

The remainder of this summary includes studies published since the Cochrane Review.

Neural Tissue Mobilization

II

In a systematic review of literature, Basson et al[34] investigated the use of neurodynamic mobilization for the treatment of neuro-musculoskeletal conditions, including CTS. The authors analyzed 12 papers evaluating the effect of neural mobilization in individuals with CTS; only 3[215, 253, 296] of which were published after the Cochrane review[223] described above. Meta-analysis was performed on patient-reported outcome measures including pain VAS (WMD=-0.22 95% CI -0.74, 0.30) and the DASH questionnaire (WMD=-1.55 95% CI -7.84, 4.75). Clinical outcome measures included timed Phalen's test (relative effect=0.81 95% CI 0.87, 1.86), grip strength (relative effect=1.18 95% CI -1.29, 3.66) and 2PD (relative effect=0.36 95% CI -0.8, 0.08). Basson et al[34] found high or uncertain risk of bias in 7 of the 12 studies and small ESs and large CIs reflecting bi-directional effects. Authors concluded the evidence did not support the effectiveness of neural mobilization for improving clinical outcomes in patients with CTS.

II

Wolny and Linek[294] studied the effects of neurodynamic techniques (provided twice weekly for 10 weeks) versus no treatment in individuals with mild or moderate CTS (n=103). Outcome measures included NCS parameters, a numeric pain rating scale (NPRS), grip and pinch strength, the CTQ-SSS and CTQ-FS. Measurements were taken at baseline and 10 weeks. Authors reported statistically significant differences between the treatment and control groups in SNCV (MD=12.4 95% CI 9.1, 15.6), DML (MD=.92 95% CI .58, 1.23), NPRS (MD=4.08 95% CI 3.73, 4.43), CTQ-SSS (MD=1.79 95% CI .91, 1.31), and CTQ-FS (MD=.91 95% CI .78, 1.24) in favor of the neurodynamic techniques. The same authors found similar results in another study comparing the effects of neurodynamic treatment to a sham nerve gliding technique (n=150).[295] Differences between groups were as follows: SNCV (MD=14.7 95% CI 10.5, 15.9), 2PD (long finger) (MD=2.38 95% CI 2.65, 2.09), DML (MD=.90 95% CI 1.15, .63), NPRS (MD=4.0 95% CI 4.28, 3.71), CTQ-SSS (MD=1.09 95% CI 1.27, .93), and CTQ-FS (MD=1.15 95% CI 1.27, .91). Adverse effects were not reported.

Massage

II

In a recent study, Madenci et al[176] investigated the addition of "Madenci hand massage" to a treatment program of night orthosis use and tendon and nerve glides in 84 individuals with mild-to-moderate severity CTS. In this non-blinded RCT, all participants wore prefabricated orthoses positioned in 0-15° of wrist extension and performed staged tendon exercises and nerve gliding exercises described by Akalin et al.[3] The experimental group also received a daily, 3-minute massage which consisted of effleurage, friction, petrissage, and shaking. Outcome measures included pain ratings: patient global assessment (PGA) and physician global assessment

(MDPGA), grip strength, DML, motor and SNCV, and the CTQ scales. At 6 weeks, both groups demonstrated improved outcomes, but the experimental group was significantly improved compared to the control group on PGA (MD=-6.2 vs. -4.1; P=.001), MDPGA (MD=-4.7 vs. -2.4; P=.001), right grip strength (MD=4.9 vs. 2.5 P=.042), left grip strength (MD=5.7 kgs vs. 3.6 kgs; P=.041), CTQ-SSS (MD=-2.8 vs -1.2 P=.001), and CTQ-FS (MD=-1.2 vs -.6; P=.001). There were improvements favoring the massage in NCS (DML, SNCV) that were not present in the control group, but they did not reach statistical significance.[176] There was no discussion of adverse effects. The results should be interpreted with caution due to the opportunity for bias (lead author invented the massage technique and chose the participating individuals), lack of non-intervention group, and confounded interventions masking the effect of a single intervention.

Manual Therapy

II

Bongi et al[43] investigated the effect of biweekly manual therapy on 22 participants (41 hands) with CTS of all severity levels using a repeated-measures, crossover design. In the initial phase, 9 participants (16 hands) were tested on all outcome measures and followed without intervention for 12 weeks and then reassessed. Outcome measures included CTQ-SSS, CTQ-FS, sensory NCV, DML, severity and clinical signs including presence of pain, night waking frequency, hypoesthesia, strength, Phalen test time, hand sensitivity, and thenar muscle atrophy. There were no significant differences on any outcome measures in this phase except the number of hands with a positive Phalen test increased from 6 to 11 (P=.0041). While 16 hands were in the control group, data were only provided on 14 hands. Participants then entered the treatment phase and received two, 45-minute sessions of education including activity modifications for performing work and home tasks followed by manual therapy sessions twice per week for 3 weeks. Manual therapy techniques included soft tissue and joint mobilization performed by the same provider. Outcome measures were assessed at 3 and 24 weeks following the initial treatment. For both data collection periods, CTQ-SSS scores improved (3-week MD=-8.14 and 24-week MD=-4.49; P<.05). The CTQ-FS score changes were also improved (3-week MD=-3.78 and 24-week MD=-3.12 (P<.05). There were no differences in nerve conduction or DML at 3 or 24 weeks. Reports of paresthesia, pain, night waking, and hand sensitivity improved significantly (P<.05) after 3 weeks. At 24 weeks, some scores showed regression yet remained improved over the baseline scores, however no statistical comparisons were reported for clinical signs. No methodology was provided on how pain and paresthesia were measured. It is unclear whether improvements were due to the manual therapy or activity modifications.

Manual Therapy versus Surgery

II

Fernández-de-las Peñas et al[94] compared manual therapy interventions to carpal tunnel decompression in 94 women diagnosed with CTS in a randomized, single-blinded trial. Manual therapy and cervical muscle stretches were performed during 30-minute sessions once per week for 3 weeks. Surgical decompression was either open or endoscopic, depending on patient and surgeon preference. Individuals treated with surgery received an educational session for performing the cervical muscle stretches. Outcome measures included the CTQ-FS, the CTQ-

SSS, cervical range of motion, and tip pinch strength (thumb-to-index and thumb to small fingers). Outcomes were measured at 0, 1, 3, 6, and 12 months post intervention. The authors reported statistically significant differences between groups on the CTQ-FS (MD=0.6 95% CI 0.45, 0.75), thumb-to-index pinch strength (MD=2.2 95% CI 1.8, 2.6), and thumb-to-little pinch strength (MD=0.8 95% CI 0.5, 1.1) at 1 month favoring manual therapy. Authors reported large ESs (1.6 and 1.1). Otherwise, both groups showed similar improvements on all variables at all data collection time points. Authors reported there were no adverse effects or post-operative complications.[94]

II

Fernández-de-las Peñas et al[96] compared manual therapy interventions to carpal tunnel decompression in 111 women diagnosed with CTS in a randomized, single-blinded trial. Manual therapy was performed for 30 minutes, once per week for 3 weeks and treatment varied based on clinical findings and provider judgement and could include vertebral glides, soft tissue and neural mobilization, and tendon gliding. Surgical decompression was either open or endoscopic, depending on patient and surgeon preference. Outcome measures were average pain, worst pain NPRS, CTQ-SSS, CTQ-FS, and Global Rating of Change (GROC) and were measured at 0, 1, 3, 6, and 12 months post intervention. At 1 and 3 months post treatment, the manual therapy group reported greater pain reduction (MD=-3.4 vs -1.5 and MD=-3.7 vs MD=-2.4, respectively) with a large ES favoring manual therapy (1.1>standard MD (SMD)>1.8). CTQ-FS scores at 1 month and 3 months also favored the manual therapy group with SMD=1.2 (large ES) and 0.8 (medium ES), respectively. No significant differences between groups were found at any point for the CTQ-SSS or at 6 or 12 months for pain or the CTQ-FS. Reported ESs for groups pre an post-treatment were large for both groups (SMD>1.3). GROC was similar for both groups at 6 (P=.663) and 12 months (P=.169). Authors reported there were no clinically important adverse events or surgical complications.[96]

Evidence Synthesis and Clinical Rationale

Evidence on the use of neurodynamic techniques is conflicting. The evidence supporting manual therapy interventions is limited by potential for bias, lack of control groups, and non-uniformity in examination and intervention techniques, sometimes within the same study. Early advantages of manual therapy compared to surgical intervention are most likely due to postoperative healing leading to greater short-term pain and dysfunction in surgically managed individuals. The decision to use manual therapy should be based on patient preference and therapist experience. Clinicians must discontinue any massage or manual therapy intervention if symptoms increase or do not improve. While no adverse effects were reported from either surgery or a variety of manual therapies in these studies, surgical complications have been reported elsewhere in this guideline.

Gaps in knowledge

There is a need for high-quality randomized controlled studies using valid, condition-appropriate outcome measures comparing specific, reproducible, manual therapy interventions to identify the most effective techniques and the appropriate dosage. Use of control groups, blinded assessors, uniform interventions, and evaluation of long-term outcomes are needed. There is no evidence that neural mobilization increases longitudinal, lateral, or anterior-posterior movement of the median nerve in the carpal tunnel in individuals with carpal tunnel syndrome or that an increase in movement is associated with a reduction in carpal tunnel pressure or carpal tunnel symptoms.

Recommendations

C

Clinicians may recommend massage for individuals with mild-to-moderate carpal tunnel syndrome in the short-term.

C

Clinicians may recommend manual therapy for individuals with mild-to-moderate carpal tunnel in the short term.

D

There is conflicting evidence on the use of neurodynamic mobilizations in the management of mild or moderate CTS.

THERAPEUTIC EXERCISE

Stretching

II

Baker et al[29] examined 4 different orthosis-stretching combinations and progression to surgery in 103 participants with mild-to-moderate CTS without thenar atrophy and normal 2PD. Participants were randomized into 4 different treatment protocols that combined orthotic intervention and stretching. Individuals wore 1 of 3 orthosis designs during sleep (a custom-fabricated orthosis with the wrist at 0° and the MP joints at 0-10° [lumbrical orthosis] or 1 of 2 prefabricated wrist orthoses [general orthosis]) and were randomly assigned to 1 of 2 stretching groups (lumbrical stretches or general stretches) to be done 6 times per day. Outcome measures were the CTQ-SSS, CTQ-FS, and the DASH, and authors determined the clinically important change (CIC) for the instruments as -.16, -.47 and -20.9 points, respectively. There was a significant main effect for time for all groups and all time points (P<.001). Two-way interactions, including orthosis x time and stretch x time, were not significant at any time point for any measure. At 12-weeks, there were significant orthosis x stretch x time interactions for the CTQ-FS and the DASH questionnaire. Post-hoc analysis showed the lumbrical orthosis/general stretch and general orthosis/lumbrical stretch were significantly improved compared to the lumbrical orthosis/lumbrical stretch for CTQ-FS, and the lumbrical orthosis/general stretch was significantly improved compared to the lumbrical orthosis/lumbrical stretch for the DASH. There were no significant 3-way interactions at 4 or 24 weeks.

When considering CIC for CTQ-SSS, CTQ-FS, and DASH in the Baker et al[29] study, at 4 weeks, 66%, 34%, and 8% of participants demonstrated a CIC, respectively. At 12 weeks, 68%, 37%, and 18% of participants reached a CIC, respectively, and at 24 weeks, 72%, 41%, and 22% reached CIC, respectively. At 24 weeks 25.5% of participants progressed to surgery with no difference between groups. No intervention was shown to be superior, and the absence of a control group and the use of multiple interventions prevents recommending one intervention. No adverse effects were reported.

Gaps in knowledge

More evidence is needed on the effects of general and lumbrical muscle stretching in individuals with CTS that include a control group. Studies are needed that examine the effects of stretching versus other types of exercise. Studies examining the combined effects of stretching and orthoses versus orthoses alone are also needed.

Recommendation

C

Clinicians may use a combined orthotic/stretching program in individuals with mild-to-moderate carpal tunnel syndrome who do not have thenar atrophy and have normal 2-point discrimination. Clinicians should monitor those undergoing treatment for clinically significant improvement.

Decision Tree:

Component 1: Examination

SUBJECTIVE HISTORY

- Demographic information
- Medical history
- Risk factor assessment
- Medical or diagnostic testing including electrodiagnostics
- Social and work history
- Symptom assessment including duration, frequency, intensity, and type
- Symptom onset (rapid or gradual)
- Presence of nocturnal symptoms
- Location of symptoms (Is sensation over scaphoid tubercle spared?)
- Activities that increase/decrease symptoms
- Chief complaint(s) including impairments, activity limitations, and participation restrictions
- Prior treatment and its success
- CTQ-SSS
- CTQ-FS or DASH Questionnaire

REVIEW OF SYSTEMS

- Cardiovascular and Pulmonary system (heart rate, blood pressure, etc.)
- Integumentary system (trophic changes, scars, discoloration, swelling,)
- Musculoskeletal system (cervical and upper quarter movement analysis, postural assessment, presence of atrophy especially thenar)
- Neuromuscular system (upper quarter screening including dermatomes and sensation in terminal branch distributions, myotomes, deep tendon reflexes, and pathological reflexes)
- Cognition and communication

TESTS AND MEASURES
When CTS is Suspected:

- Phalen test
- Assess for presence of Tinel sign
- Monofilament threshold testing
- Static 2-point discrimination
- Baseline grip and pinch strength
- Dellon-modified Moberg pick-up Test
- Abductor pollicis brevis weakness
- Test combination looking for 3 or more of the following: *shaking hands provide relief, wrist ratio > .67, CTQ-SSS >1.9, diminished light touch in median nerve distribution*

Component 2: Medical Screening
Following the examination, therapists should choose one of the following actions:

Patient/client is appropriate for physical therapy services and provides an evidence-based intervention

- Examination data show findings consistent with mild-to-moderate CTS and the patient/client is in agreement with a trial of conservative management

- Examination data show findings consistent with severe CTS *and* the patient/client has seen a surgeon who has decided he or she is not a surgical candidate due to co-morbidities, or the patient/client is awaiting surgery, *or* the patient/client has refused surgery after counseling on the negative effects of long-standing nerve compression

Patient/client is appropriate for physical therapy but would benefit from a referral to an additional provider

- Examination data suggest any severity CTS with concurrent signs and symptoms of another condition that warrant further medical testing. In these individuals, CTS treatment may commence as long as there would be no contraindications with suspected concurrent condition.

- Examination data suggest signs and symptoms consistent with severe CTS and the patient/client chooses a trial of conservative intervention while awaiting physician visit.

Patient is not appropriate for physical therapy and requires referral to another provider

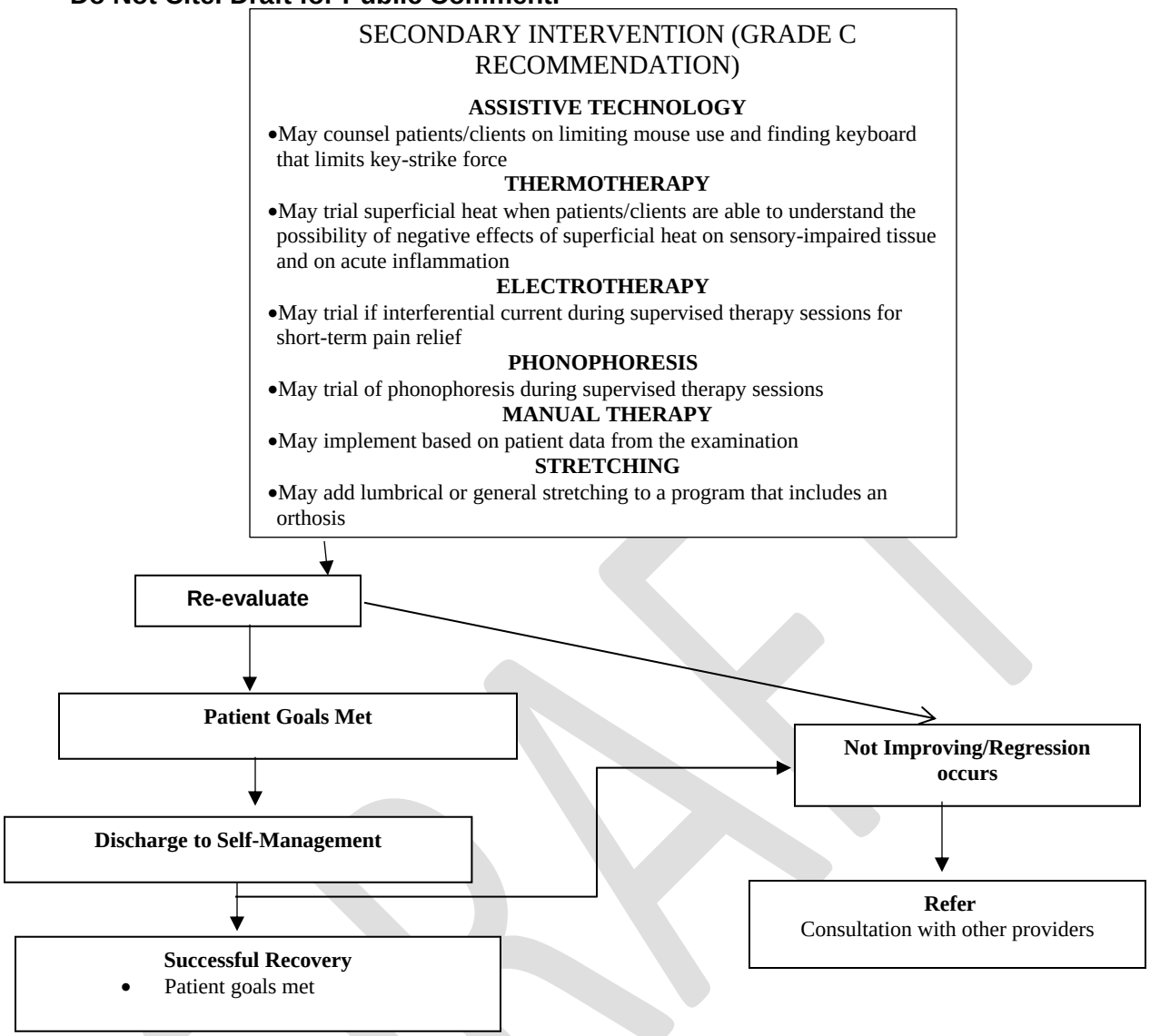
- Examination data reveals suspected neuromuscular diagnosis other than CTS that is beyond the scope of physical therapy treatment

Component 3: Intervention Strategies

ORTHOSES

PRIMARY INTERVENTION (GRADE B RECOMMENDATION)

- Patients/clients should be instructed in the use of a neutrally-positioned wrist orthosis for night wear. Treatment should also include counseling on pathology, risk identification, symptom self-management, and postures/activities that aggravate symptoms. Duration of orthosis use may be increased to include daytime wear or the metacarpophalangeal joints may be included if night-time wrist-neutral positioning alone does not provide sufficient relief.



List of Acronyms

CTS: carpal tunnel syndrome; CTQ-FS: Carpal Tunnel Questionnaire-Functional Scale; CTQ-SSS: Carpal Tunnel Questionnaire-Symptom Severity Scale; DASH: Disabilities of the Arm, Shoulder and Hand

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APPENDIX A. SEARCH STRATEGIES FOR ALL DATABASES SEARCHED

Medline and CINAHL

("carpal tunnel syndrome" OR "median nerve compression") AND (incidence OR prevalence) AND (2008 [PDat] : 2018 [PDat]; ("carpal tunnel syndrome" OR "median nerve compression") AND (pathology OR pathophysiology OR pathoanatomy OR histo*); "carpal tunnel pressure"; ("carpal tunnel syndrome" OR "median nerve compression") AND classification; ("carpal tunnel syndrome" OR "median nerve compression") AND (inflammation OR prostaglandin); ("carpal tunnel syndrome" OR "median nerve compression") AND conservative AND (outcome OR "clinical course")

("carpal tunnel syndrome" OR "median nerve compression") AND "self-report measures"; ("carpal tunnel syndrome" OR "median nerve compression") AND "patient-report measures"; ("carpal tunnel syndrome" OR "median nerve compression") AND "internal consistency"; ("carpal tunnel syndrome" OR "median nerve compression") AND reliability; ("carpal tunnel syndrome" OR "median nerve compression") AND validity; DASH AND ("carpal tunnel syndrome" OR "median nerve compression"); DASH AND "psychometric properties"; "Katz hand diagram" AND ("carpal tunnel syndrome" OR "median nerve compression"); "Brigham & Women's Hospital carpal tunnel questionnaire"; "6-item carpal tunnel syndrome symptoms scale"; QuickDASH AND ("carpal tunnel syndrome" OR "median nerve compression"); QuickDASH AND "psychometric properties"; "Palmar pain scale" AND ("carpal tunnel syndrome" OR "median nerve compression"); "Palmar pain scale" AND "psychometric properties"; "Boston carpal tunnel questionnaire"; "Boston carpal tunnel questionnaire" AND "psychometric properties"; "Michigan hand outcome questionnaire" AND ("carpal tunnel syndrome" OR "median nerve compression"); "Michigan hand outcome questionnaire" AND "psychometric properties"; "patient evaluation measure" AND ("carpal tunnel syndrome" OR "median nerve compression"); SF-36 AND ("carpal tunnel syndrome" OR "median nerve compression"); SF-36 AND "psychometric properties"; "patient-rated wrist evaluation questionnaire" AND ("carpal tunnel syndrome" OR "median nerve compression"); "patient-rated wrist evaluation questionnaire" AND "psychometric properties"; "upper extremity functional scale" AND ("carpal tunnel syndrome" OR "median nerve compression"); "upper extremity functional scale" AND "psychometric properties"; "Mcgill pain questionnaire" AND ("carpal tunnel syndrome" OR "median nerve compression"); "Flinn Performance screening tool" AND ("carpal tunnel syndrome" OR "median nerve compression"); "7 item satisfaction scale AND ("carpal tunnel syndrome" OR "median nerve compression"); "12 item brief Michigan hand questionnaire" AND ("carpal tunnel syndrome" OR "median nerve compression")

"Impairment measures" AND ("carpal tunnel syndrome" OR "median nerve compression"); "functional outcome measures" AND ("carpal tunnel syndrome" OR "median nerve compression"); "internal consistency" AND ("carpal tunnel syndrome" OR "median nerve compression"); reliability AND ("carpal tunnel syndrome" OR "median nerve compression"); validity AND ("carpal tunnel syndrome" OR "median nerve compression")

("carpal tunnel syndrome" OR "median nerve compression") AND "grip strength" AND "measurement"; ("carpal tunnel syndrome" OR "median nerve compression") AND "grip strength" AND "reliability"; ("carpal tunnel syndrome" OR "median nerve compression") AND "grip strength" AND "measurement" and "standardization"; ("carpal tunnel syndrome" OR "median nerve compression") AND "grip strength" AND "minimal detectable change". ("carpal

tunnel syndrome" OR "median nerve compression") AND "grip strength" AND "clinically relevant change". ("carpal tunnel syndrome" OR "median nerve compression") AND "grip strength" AND "responsiveness." The same strategy was used for fingertip pinch, lateral pinch, tripod pinch, manual muscle testing, abductor pollicis brevis strength, range of motion, Grooved Peg Board Test, Functional Dexterity Test, Minnesota Manual Dexterity Test, Minnesota Rate of Manipulation, Moberg Pick Up Test, Purdue Peg Board, 9-hole Peg Test, Jebsen–Taylor Hand Function Test, NK Dexterity Test, Bennett Hand Tool Dexterity Test, Box and Block Test, O'Neil Hand Function Assessment, Rosenbusch Test of Finger Dexterity, Radboud Skills Test, Sequential Occupational Dexterity Test, Smith Hand Function Evaluation, Sollerman Hand Function Test; Southhampton Hand Assessment Procedure; Upper Extremity Functional Test; Hand Function Sort; Crawford Small Parts Dexterity Test; Valpar Worksample, shape-texture identification, vibration, sensory testing, Semmes Weinstein Monofilaments, static and moving 2-point discrimination.

("carpal tunnel syndrome" OR "median nerve compression") AND ("risk factors"); ("carpal tunnel syndrome" OR "median nerve compression") AND (obesity); ("carpal tunnel syndrome" OR "median nerve compression") AND "Body Mass Index"); ("carpal tunnel syndrome" OR "median nerve compression") AND (hypothyroidism OR "Thyroid dysfunction" OR "Graves disease'; ("carpal tunnel syndrome" OR "median nerve compression") AND ("Female gender"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("diabetes mellitus"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("rheumatoid arthritis"); ("carpal tunnel syndrome" OR "median nerve compression") AND (osteoarthritis); ("carpal tunnel syndrome" OR "median nerve compression") AND (anthropometrics); ("carpal tunnel syndrome" OR "median nerve compression") AND ("square wrist"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("hand dimensions"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("hand shape"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("family history"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("genetic predisposition"); ("carpal tunnel syndrome" OR "median nerve compression") AND (height); ("carpal tunnel syndrome" OR "median nerve compression") AND (alcohol); ("carpal tunnel syndrome" OR "median nerve compression") AND (smoking OR tobacco);("carpal tunnel syndrome" OR "median nerve compression") AND ("physical activity"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("hormone therapy" OR "oral contraceptives" OR "estrogen"); ("carpal tunnel syndrome" OR "median nerve compression") AND (hysterectomy OR menopause OR oophorectomy); ("carpal tunnel syndrome" OR "median nerve compression") AND (parity); ("carpal tunnel syndrome" OR "median nerve compression") AND (occupational risk factors); ("carpal tunnel syndrome" OR "median nerve compression") AND ("forceful exertions");); ("carpal tunnel syndrome" OR "median nerve compression") AND (repetition); ("carpal tunnel syndrome" OR "median nerve compression") AND ("repetitive work"); ("carpal tunnel syndrome" OR "median nerve compression") AND (vibration); ("carpal tunnel syndrome" OR "median nerve compression") AND ("wrist position"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("computer use" OR "keyboard use" or "mouse use"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("psychosocial factors")

("carpal tunnel syndrome" OR "median nerve compression") AND (intervention OR treatment NOT surgical); ("carpal tunnel syndrome" OR "median nerve compression") AND ("physical therapy" OR "occupational therapy'); ("carpal tunnel syndrome" OR "median nerve compression") AND (orthoses OR orthosis OR splinting); ("carpal tunnel syndrome" OR

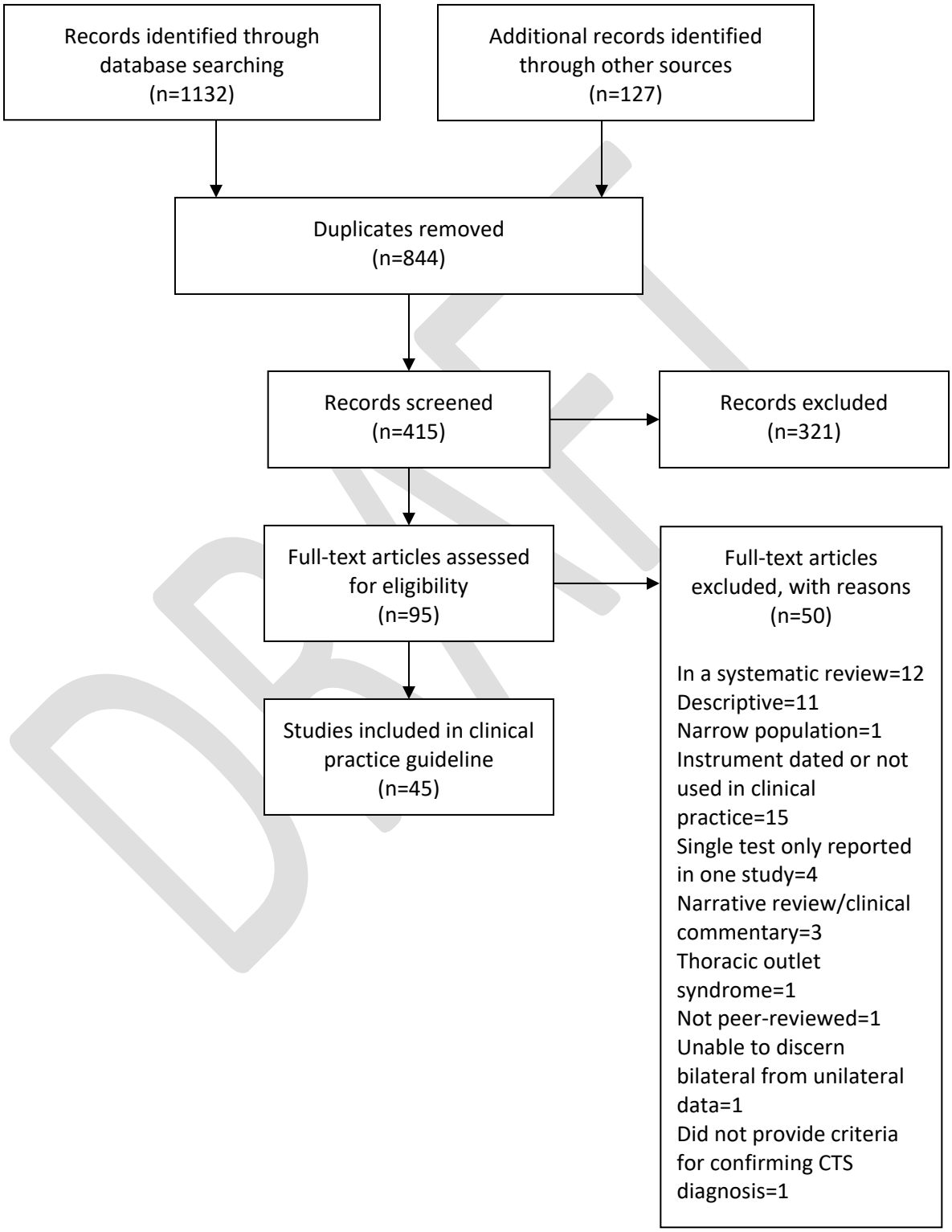
"median nerve compression") AND education; ("carpal tunnel syndrome" OR "median nerve compression") AND ergonomics; ("carpal tunnel syndrome" OR "median nerve compression") AND ("electrical stimulation" OR "TENS"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("dry needling"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("low level laser therapy"); ("carpal tunnel syndrome" OR "median nerve compression") AND (iontophoresis OR phonophoresis); ("carpal tunnel syndrome" OR "median nerve compression") AND (massage OR "myofascial release"); ("carpal tunnel syndrome" OR "median nerve compression") AND (mobilization OR "soft tissue mobilization" OR "joint mobilization"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("nerve gliding" OR "tendon gliding"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("chiropractic treatment"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("postural training"); ("carpal tunnel syndrome" OR "median nerve compression") AND (exercise OR yoga OR Pilates); ("carpal tunnel syndrome" OR "median nerve compression") AND (heat OR "thermal modalities" OR paraffin); ("carpal tunnel syndrome" OR "median nerve compression") AND ("short wave diathermy or "microwave diathermy"); ("carpal tunnel syndrome" OR "median nerve compression") AND ("therapeutic exercise"); ("carpal tunnel syndrome" OR "median nerve compression") AND (ultrasound).

("carpal tunnel syndrome" OR "median nerve compression") AND diagnosis; ("carpal tunnel syndrome" OR "median nerve compression") AND Tinel; ("carpal tunnel syndrome" OR "median nerve compression") AND Phalen; ("carpal tunnel syndrome" OR "median nerve compression") AND carpal-compression; AND ("carpal tunnel syndrome" OR "median nerve compression") AND upper-limb-neurodynamic; ("carpal tunnel syndrome" OR "median nerve compression") AND scratch-collapse; ("carpal tunnel syndrome" OR "median nerve compression") AND monofilament; ("carpal tunnel syndrome" OR "median nerve compression") AND threshold; ("carpal tunnel syndrome" OR "median nerve compression") AND Semmes-Weinstein; ("carpal tunnel syndrome" OR "median nerve compression") AND two-point; ("carpal tunnel syndrome" OR "median nerve compression") AND vibrat*; ("carpal tunnel syndrome" OR "median nerve compression") AND finger-flexion; ("carpal tunnel syndrome" OR "median nerve compression") AND Luthy; ("carpal tunnel syndrome" OR "median nerve compression") AND lunate-press; ("carpal tunnel syndrome" OR "median nerve compression") AND pneumatic-compression; ("carpal tunnel syndrome" OR "median nerve compression") AND Tanzer; ("carpal tunnel syndrome" OR "median nerve compression") AND tethered-median-nerve

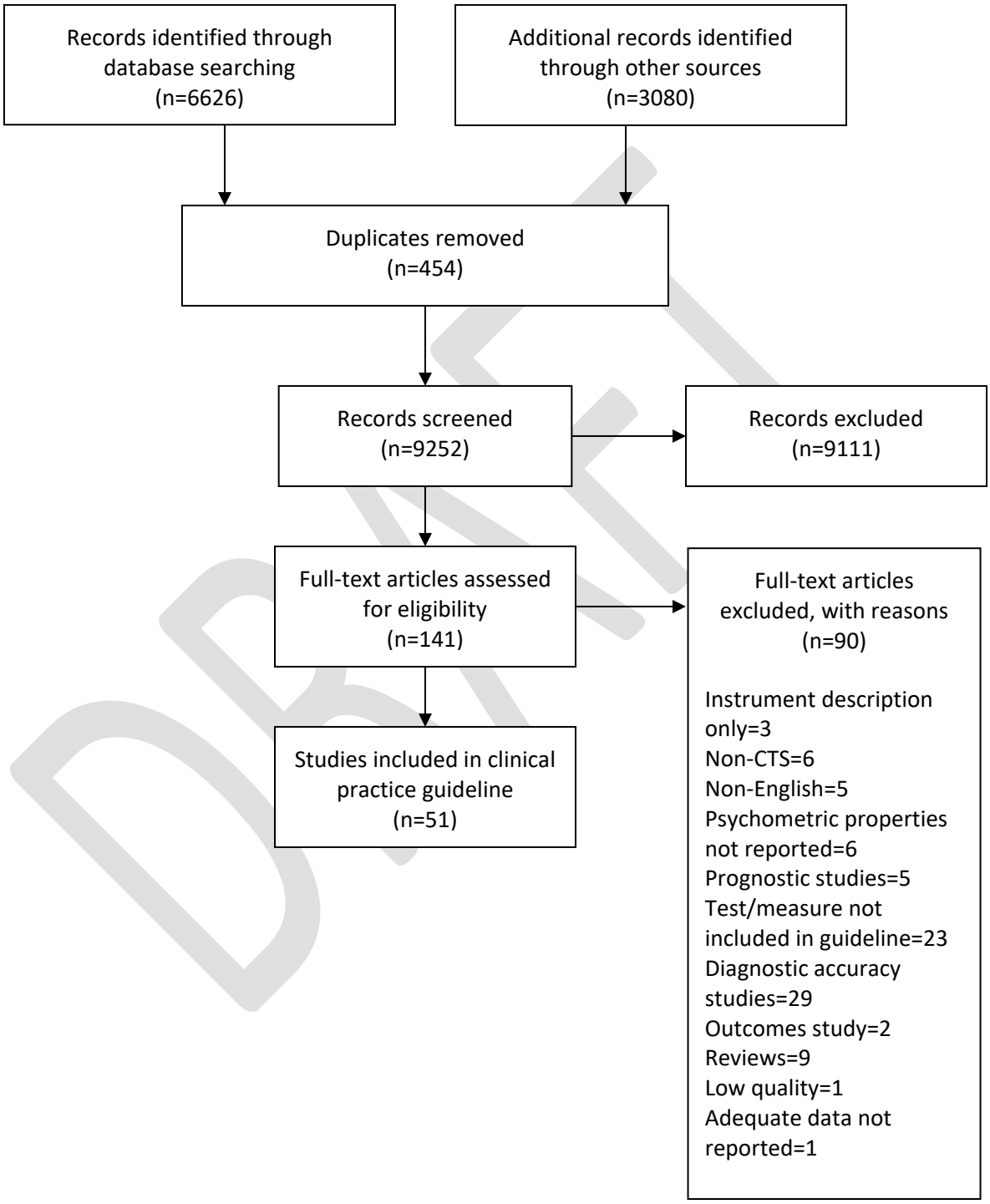
Cochrane Database

"Carpal tunnel syndrome" OR "median nerve compression"

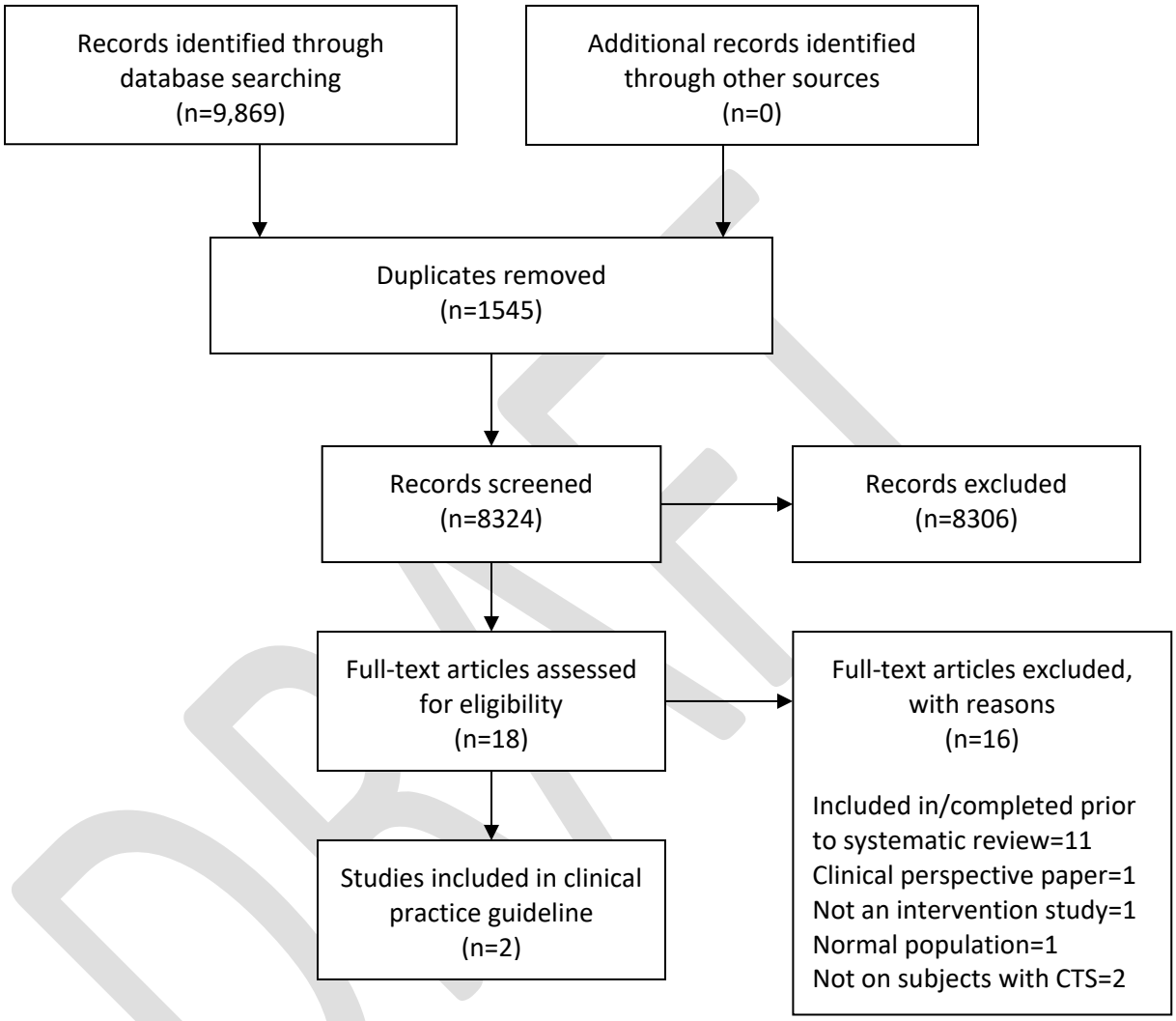
Appendix B1. PRISMA Flow Diagram. Diagnosis.



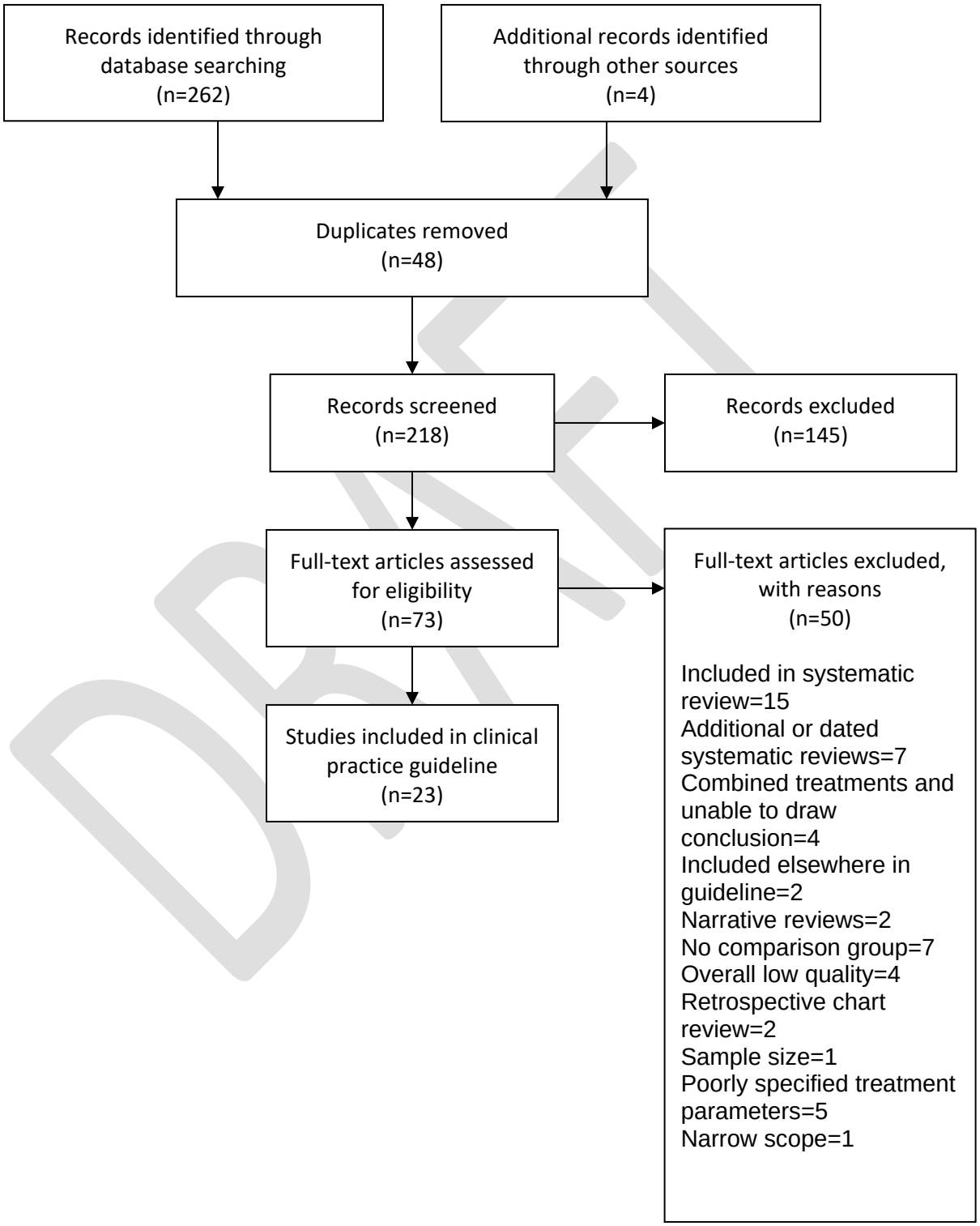
Appendix B2. PRISMA Flow Diagram. Outcomes Measures.



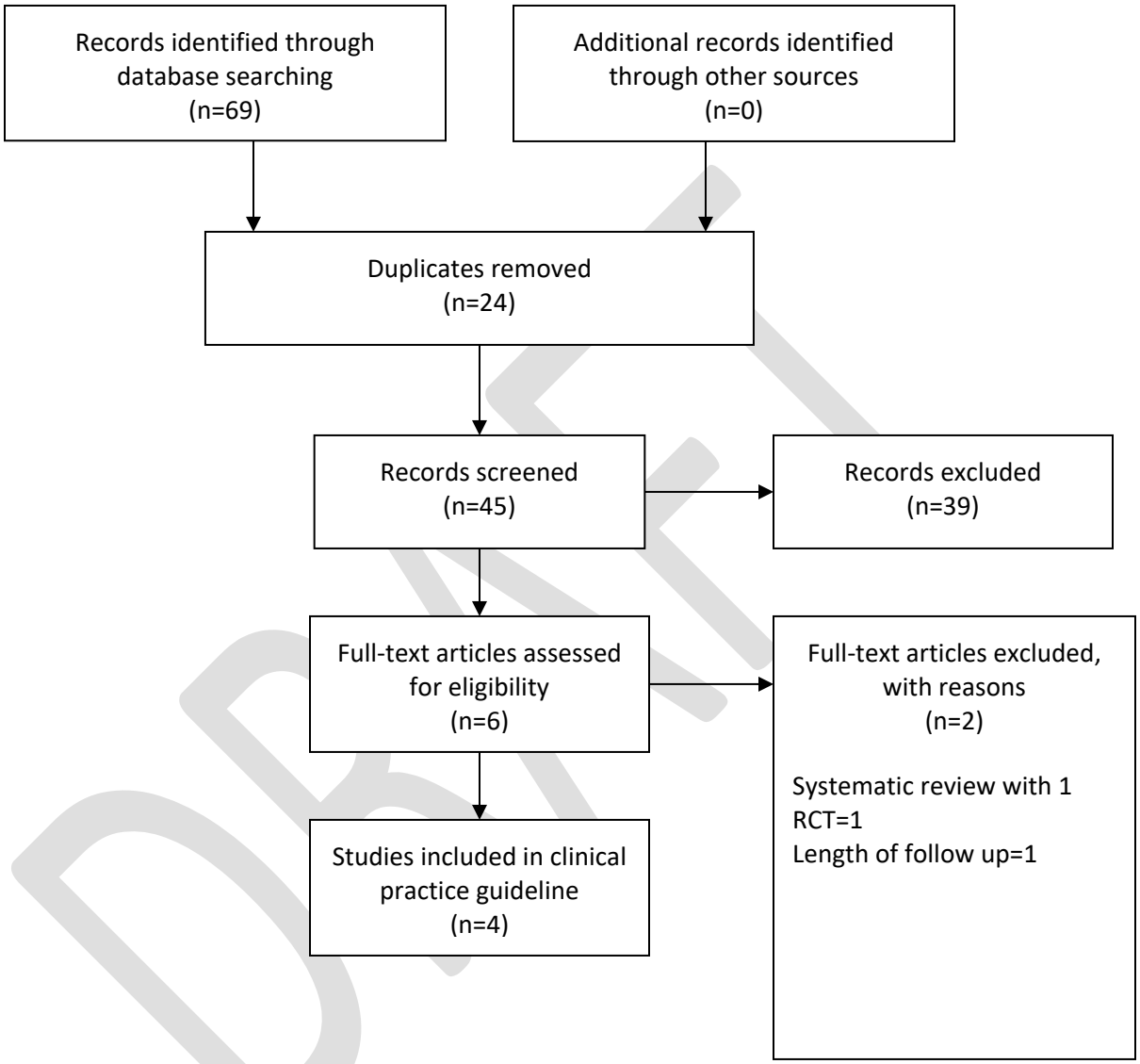
Appendix B3. PRISMA Flow Diagram. Assistive Technology.



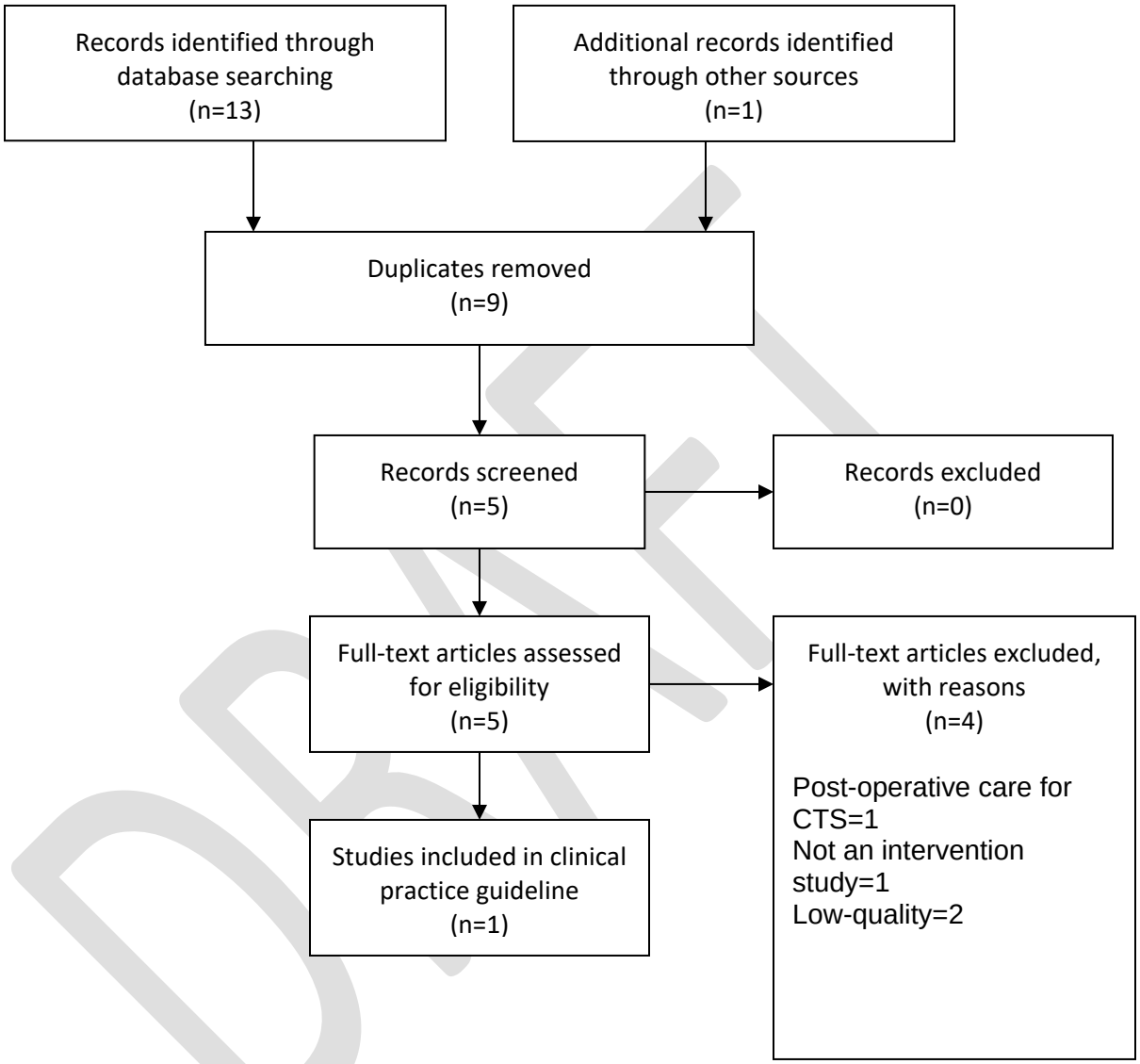
Appendix B4. PRISMA Flow Diagram. Orthoses.



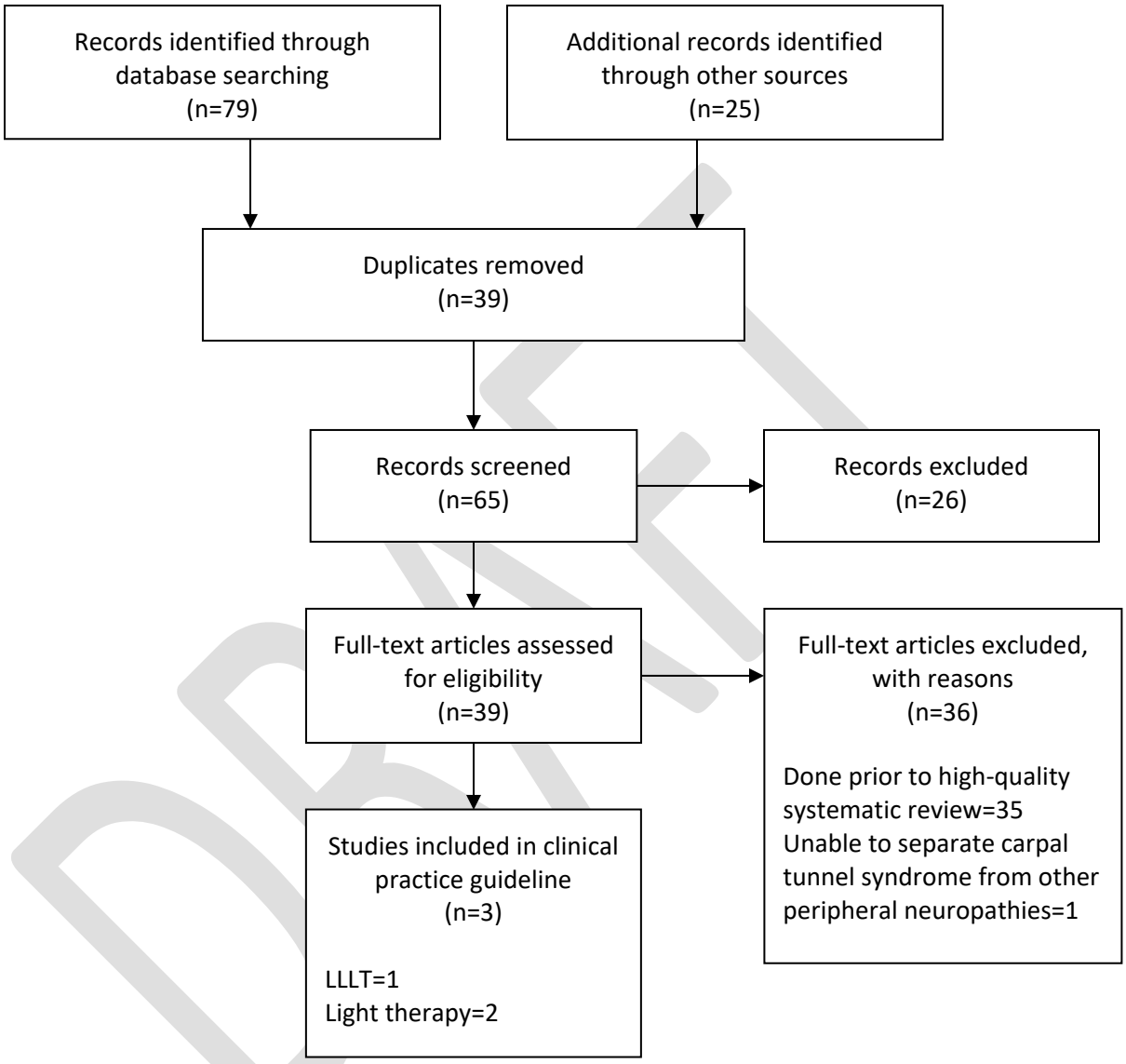
Appendix B5. PRISMA Flow Diagram. Thermotherapy.



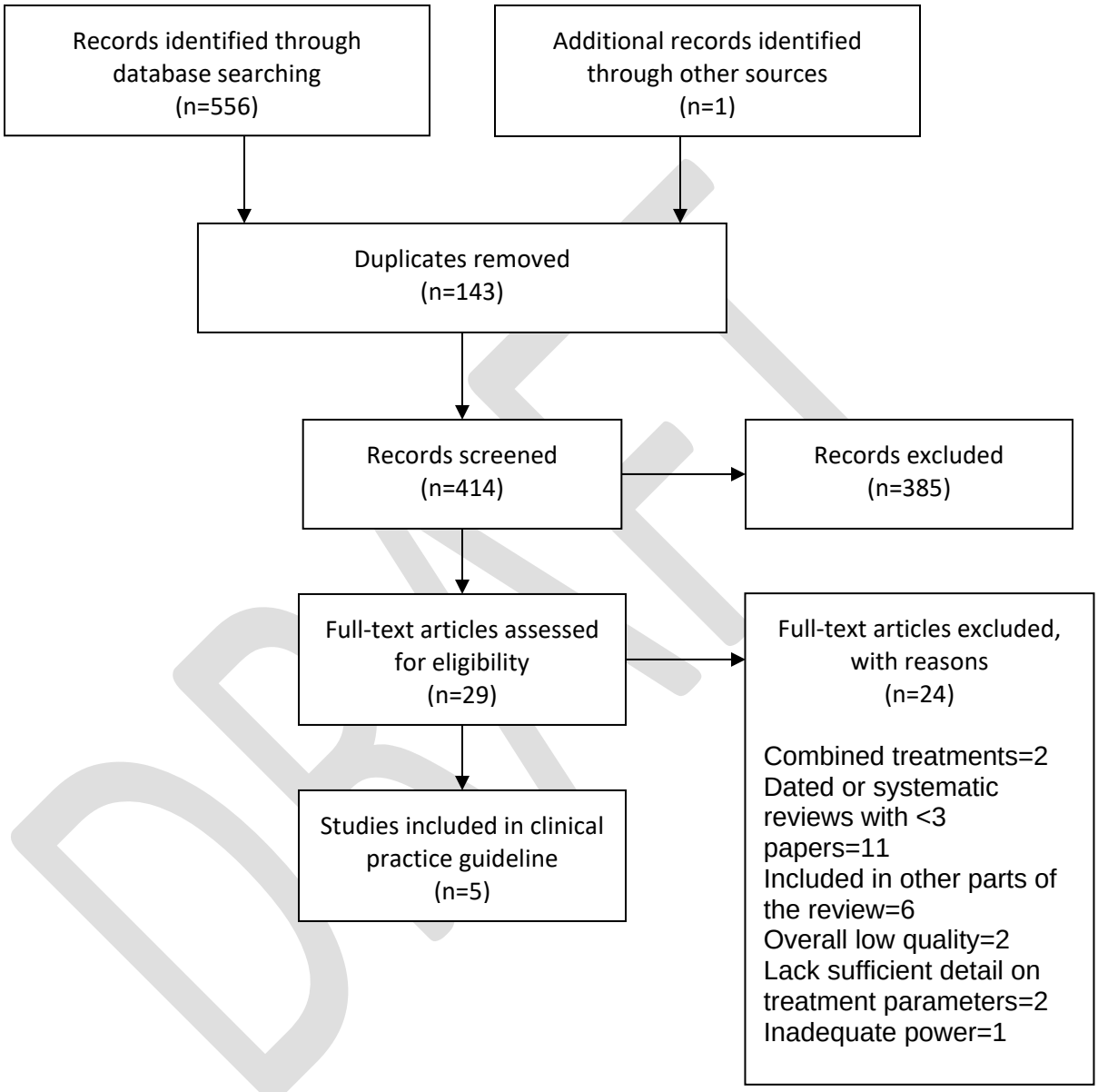
Appendix B6. PRISMA Flow Diagram. Electrotherapy.



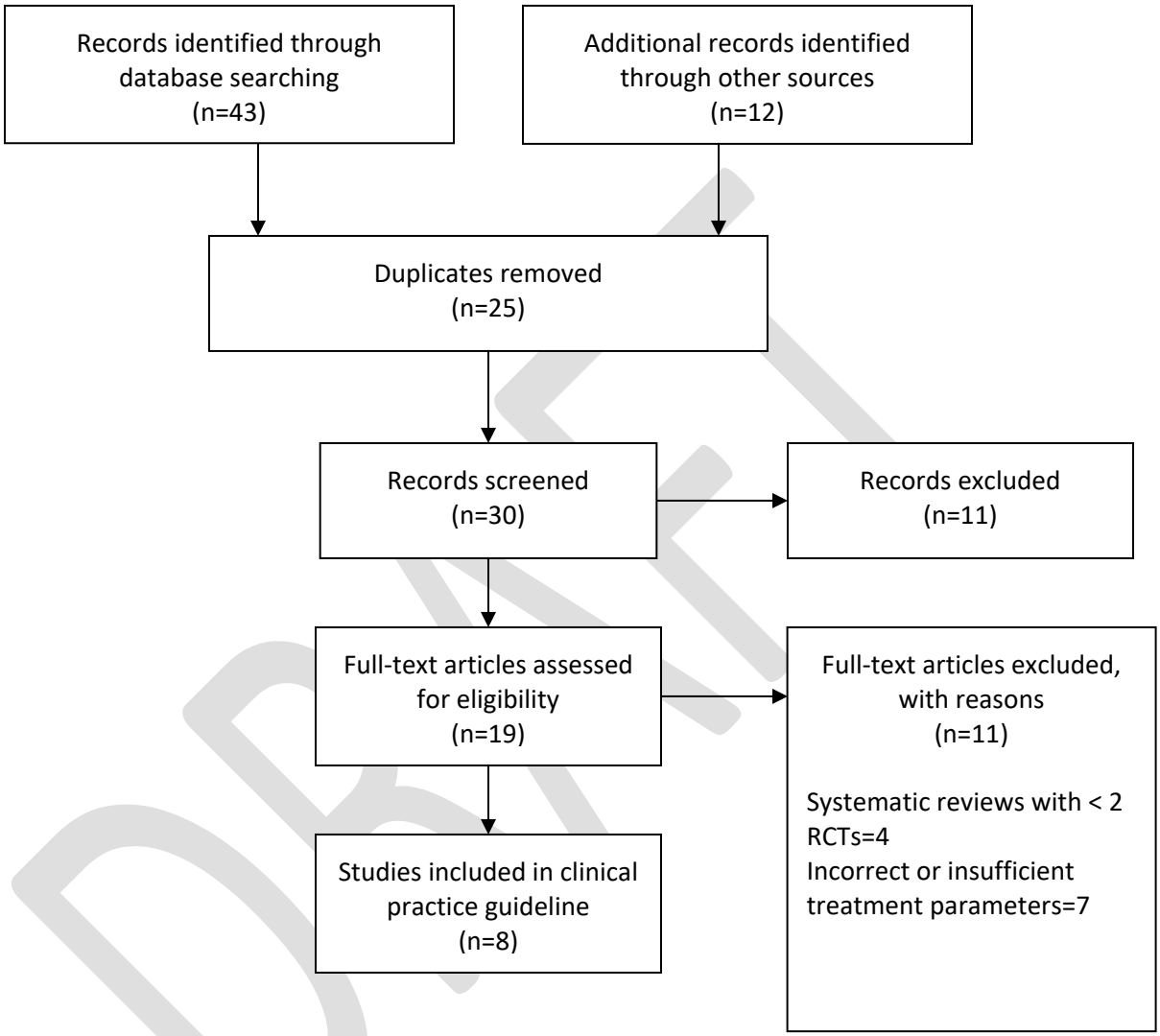
Appendix B7. PRISMA Flow Diagram. Light Agents.



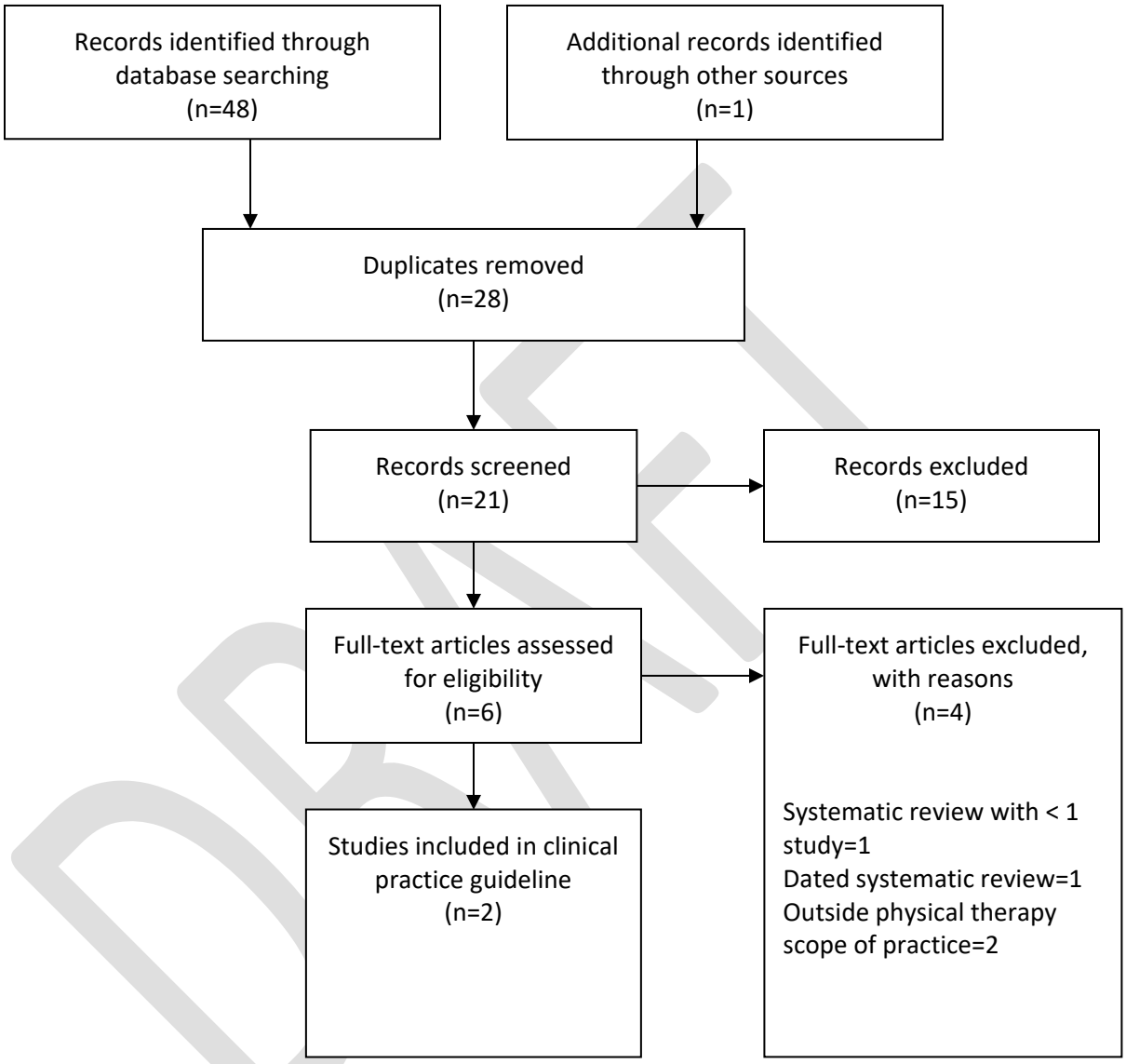
Appendix B8. PRISMA Flow Diagram. Sound Agents.



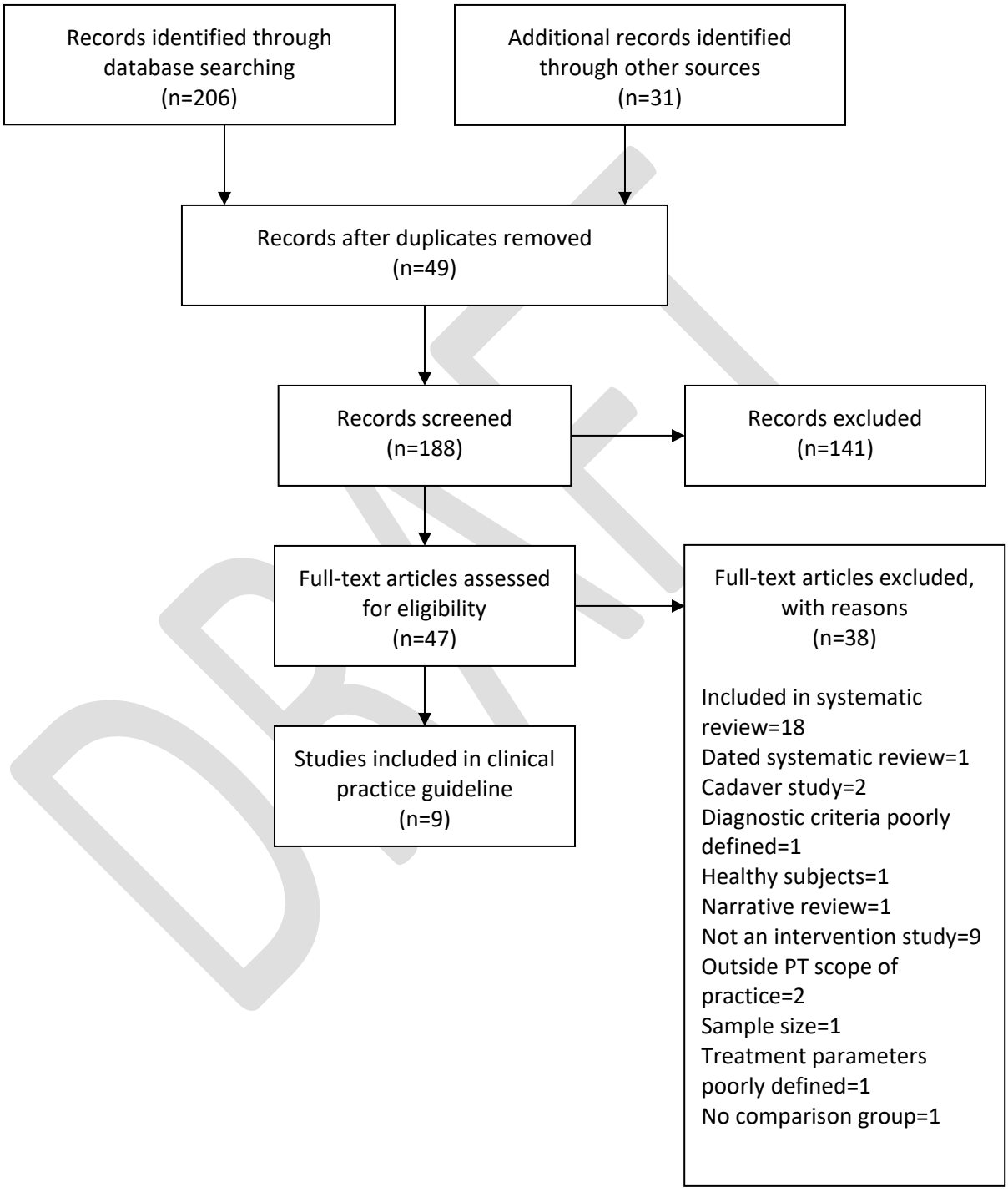
Appendix B9. PRISMA Flow Diagram. Transdermal drug delivery.



Appendix B10. PRISMA Flow Diagram. Magnet Therapy.



Appendix B11. PRISMA Flow Diagram. Manual Therapy and Stretching.



APPENDIX C. INCLUSION AND EXCLUSION CRITERIA OF STUDIES FOR REVIEW

Inclusion criteria:

We included papers that used the following research designs: systematic reviews, meta-analyses, experimental and quasi-experimental, prospective and retrospective cohort, cross-sectional, and case series studies pertaining to the following areas:

- Incidence or prevalence of carpal tunnel syndrome in the general and working populations
- Pathoanatomy of carpal tunnel syndrome
- Classification of carpal tunnel syndrome using measures other than electrodiagnostic instruments
- Identification of risk factors for carpal tunnel syndrome
- Diagnostic tests and measures for identifying carpal tunnel syndrome within the scope of physical therapist practice
- Outcome or clinical measures used to assess change in individuals with carpal tunnel syndrome, including the identification of psychometric properties
- Interventions used in the non-surgical management of carpal tunnel syndrome within the scope of physical therapist practice

We included expert review papers when they were developed using results from basic science, bench, or animal research AND when higher-level papers were not available.

Exclusion criteria:

- Studies written in a language other than English
- Studies in which the sample of patients with carpal tunnel syndrome sample cannot be separated from the remaining sample
- Studies with less than 10 participants
- Nonsystematic or narrative reviews
- Studies that included individuals with carpal tunnel syndrome who were younger than18 years old
    - Basic science, bench, cadaveric, and animal studies when higher-level human studies were available
    - Studies without a comparison group when a preponderance of higher-level studies was available
- Studies pertaining to:
    - Acute carpal tunnel syndrome
    - Induction of acute carpal tunnel symptoms in healthy individuals
    - Numbness and tingling related to diseases or conditions other than carpal tunnel syndrome, such as cervical radiculopathy and diabetic polyneuropathy
    - Tests and measures not readily or routinely available to the majority of physical therapist practitioners such as:
        - Electromyography and nerve conduction
        - Diagnostic ultrasound
        - Magnetic resonance imaging
    - Studies on ~~I~~incidence or prevalence ~~rates of studies~~ greater than 10 years old
    - Incidence or prevalence in narrow populations that limit generalizability

- Instrument measurement properties developed on a population other than those with carpal tunnel syndrome
- Interventions outside the scope of physical therapist practice such as extracorporeal shockwave therapy, prescription medications, or cortisone injections
- Interventions that were not reproducible based on the description provided by authors
- ~~Basic science, bench, cadaveric, and animal studies when higher-level human studies were available~~
- ~~Studies without a comparison group when a preponderance of higher-level studies was available~~

APPENDIX D. Critical Appraisal Scores

Provocative Tests

Study	Evaluation Criteria[a]														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
Ahn (2001)	0	1	0	0	0	0	1	1	1	0	1	1	1	1	8/14
Al-Dabbagh (2013)	0	1	0	1	0	0	1	0	0	0	1	1	0	0	5/14
Amirfeyz (2005)	0	1	0	0	0	1	1	1	1	0	0	1	0	0	6/14
Amirfeyz (2011)	0	1	0	0	0	0	1	0	1	0	1	1	0	0	5/14
Baselgia (2017)	0	1	1	1	0	0	1	1	1	1	1	0	1	1	10/14
Blok (2014)	1	1	1	1	1	0	0	1	1	1	1	1	1	1	12/14
Boland (2009)	0	1	1	1	0	0	0	1	1	0	1	1	0	0	7/14
Bueno-Garcia (2016)	1	1	1	1	1	1	1	1	1	0	1	1	1	1	13/14
Calfee et al (2012)	0	1	0	1	1	1	1	1	1	1	1	1	1	1	12/14
Cheng (2008)	0	1	0	0	0	0	1	1	1	1	1	1	1	1	9/14

El Miedany (2008)	0	1	1	1	0	0	1	1	1	0	1	1	0	0	8/14
Fertl (1998)	0	1	1	1	0	0	1	1	1	0	1	1	0	0	8/14
Goloborod'ko (2004)	0	1	0	0	0	0	0	0	0	0	1	1	1	1	5/14
Kasundra (2015)	0	1	1	1	1	1	1	0	0	0	1	1	0	0	8/14
Koris (1990)	0	1	0	1	0	0	0	1	1	0	0	0	1	0	5/14
LaJoie (2005)	0	1	1	1	1	1	1	1	1	0	1	1	1	1	12/14
Ma (2012)	0	1	0	0	0	0	1	1	1	0	1	1	1	1	8/14
MacDermid (1997)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	14/14
Makanji (2014)	1	1	1	1	1	0	0	0	0	0	1	1	1	1	9/14
Mondelli (2001)	0	1	1	1	1	1	1	1	1	0	1	1	0	0	10/14
Ntani (2013)	1	1	1	1	1	0	1	1	1	0	0	0	1	1	10/14
Thüngen 2012	1	1	1	1	1	1	1	1	1	0	1	1	0	0	11/14
Vanti (2011)	1	1	1	1	0	0	0	1	1	0	1	1	1	1	10/14
Vanti (2012)	1	1	1	0	1	0	1	1	1	0	1	1	1	1	11/14
Wainner	1	1	1	1	1	1	1	1	1	1	1	1	1	1	14/14

Williams (1992)	0	0	0	0	0	0	0	1	1	0	0	1	1	1	5/14
Wolny (2016)	0	0	1	1	0	0	1	1	0	0	0	0	1	0	5/14

[a]Law M, MacDermid J. *Evidence-based Rehabilitation: A Guide to Practice.* 3rd ed. Thorofare, New Jersey: SLACK Inc; 2014. (Scored 0=Criterion not met; 1=Criterion met): (1) Independent blind comparison with a reference standard test; (2) Reference standard/true diagnosis selected is considered gold standard or reasonable alternative; (3) Reference standard applied to all patients; (4) Actual cases included appropriate spectrum of symptom severity; (5) Non-cases might reasonable present for diagnosis; (6) Non-cases included appropriate spectrum of patients with alternative diagnosis; (7) Adequate sample size; (8) Description of the test maneuver described in sufficient detail to permit replication; (9) Exact criteria for interpreting test results provided; (10) Reliability of the test documented; (11) Number of positive and negative results reported for both cases and non-cases; (12) Appropriate statistics (sensitivity, specificity, likelihood rations) presented; (13) If test required examiner interpretation, qualifications and skills of examiner were provided; (14) Training, skills, and experience of the examiner were appropriate to the test conducted.

Katz Hand Diagram and Provocative Tests-Reliability

Study	Evaluation Criteria[a]												
	1	2	3	4	5	6	7	8	9	10	11	12	Total
Calfee et al (2012)	2	2	2	2	0	1	2	1	2	2	2	2	20/24
Marx (1998)	2	2	1	1	0	2	0	2	2	2	2	2	18/24
Priganc (2003)	2	2	1	2	0	2	2	2	2	2	2	2	21/24
Salerno (2000)	2	2	1	2	0	1	2	2	2	2	2	2	20/24

[a]Law M, MacDermid J. *Evidence-based Rehabilitation: A Guide to Practice.* 3rd ed. Thorofare, New Jersey: SLACK Inc; 2014. (Scored 0=Criterion not met; 1=Marginally meets criterion; 2=Meets criterion): (1) Comprehensive literature review to justify the research question; (2) Specific inclusion/exclusion criteria; (3) Specific hypotheses; (4) Appropriate scope of measurement properties; (5) Sample-size justification; (6) Minimal loss to follow-up; (7) Detailing the test procedures; (8) Standardization of measurement techniques; (9) Data presented for each hypothesis; (10) Appropriate statistical tests; (11) Range of analyses for each measurement property; (12) Proper presentation of the conclusions and clinical recommendations.

Sensory Testing Measures

Study	Evaluation Criteria[a]														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
Checkosky (1996)	0	1	0	0	0	0	0	1	0	0	1	1	0	0	4/14
Clark (2011)	0	1	1	0	0	0	1	1	1	0	1	1	0	0	7/14
Elfar (2010)	1	1	1	0	1	0	0	1	0	0	0	0	1	1	7/14
Gerr (1998)	1	1	1	1	1	0	1	1	1	0	1	0	1	1	11/14
Hardy (1992)	1	1	1	1	1	1	1	0	1	0	0	0	1	1	10/14
Jetzer (1991)	0	1	0	1	1	0	1	0	1	0	0	0	0	0	5/14
Kang (2008)	0	1	1	1	1	1	1	1	1	0	1	1	0	0	10/14
MacDermid (1994)	1	1	1	1	1	1	0	1	1	1	1	1	1	1	13/14
MacDermid (1997)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	14/14
Marlow (1999)	0	1	1	1	1	0	1	1	1	0	1	1	1	1	11/14

Werner (1995)	1	1	1	1	1	1	1	1	1	0	1	1	1	1	13/14
Yildirim (2015)	1	0	1	1	1	1	1	0	1	0	1	1	1	1	11/14

[a]Law M, MacDermid J. *Evidence-based Rehabilitation: A Guide to Practice.* 3rd ed. Thorofare, New Jersey: SLACK Inc; 2014. (Scored 0=Criterion not met; 1=Criterion met): (1) Independent blind comparison with a reference standard test; (2) Reference standard/true diagnosis selected is considered gold standard or reasonable alternative; (3) Reference standard applied to all patients; (4) Actual cases included appropriate spectrum of symptom severity; (5) Non-cases might reasonable present for diagnosis; (6) Non-cases included appropriate spectrum of patients with alternative diagnosis; (7) Adequate sample size; (8) Description of the test maneuver described in sufficient detail to permit replication; (9) Exact criteria for interpreting test results provided; (10) Reliability of the test documented; (11) Number of positive and negative results reported for both cases and non-cases; (12) Appropriate statistics (sensitivity, specificity, likelihood rations) presented; (13) If test required examiner interpretation, qualifications and skills of examiner were provided; (14) Training, skills, and experience of the examiner were appropriate to the test conducted.

Sensory Testing Measures--Reliability

Study	Evaluation Criteria[a]												
	1	2	3	4	5	6	7	8	9	10	11	12	Total
Cheung 2014	2	2	1	2	2	1	2	2	2	2	2	2	22/24
Grunert 1990	2	1	1	2	0	2	2	1	2	0	0	1	14/24
Hubbard 2004	2	2	1	0	0	1	2	1	2	2	2	2	17/24
Marx 1998	2	2	1	1	0	2	0	2	2	2	2	2	18/24
Raji 2014	2	2	2	2	0	2	2	1	2	2	2	2	21/24

[a]Law M, MacDermid J. *Evidence-based Rehabilitation: A Guide to Practice.* 3rd ed. Thorofare, New Jersey: SLACK Inc; 2014. (Scored 0=Criterion not met; 1=Marginally meets criterion; 2=Meets criterion): (1) Comprehensive literature review to justify the research question; (2)

Specific inclusion/exclusion criteria; (3) Specific hypotheses; (4) Appropriate scope of measurement properties; (5) Sample-size justification; (6) Minimal loss to follow-up; (7) Detailing the test procedures; (8) Standardization of measurement techniques; (9) Data presented for each hypothesis; (10) Appropriate statistical tests; (11) Range of analyses for each measurement property; (12) Proper presentation of the conclusions and clinical recommendations.

Outcome measures

Study	Evaluation Criteria[a]												
	1	2	3	4	5	6	7	8	9	10	11	12	Total
Alderson (1999)	1	1	1	1	0	1	2	2	2	2	1	1	15/24
Amadio (1996)	2	1	2	1	0	1	2	2	2	2	1	2	18/24
Amirfeyz (2009)	2	1	2	2	0	1	0	0	2	1	1	2	14/24
Amirjani et al (2011)[b]	2	2	2	1	0	0	2	2	2	2	2	2	19/24
Amirjani et al (2011)[c]	2	2	2	1	1	0	2	2	2	2	0	2	18/24
Appleby (2009)	2	2	1	1	0	2	2	2	2	2	1	1	18/24
Astifidus (2009)	2	1	2	2	2	2	2	2	2	1	0	2	20/24
Atalay (2011)	1	2	1	2	2	2	2	0	2	1	0	1	16/24
Atroshi (1999)	2	2	2	2	1	2	2	2	2	2	2	2	23/24
Atroshi (2007)	2	1	2	2	2	1	2	1	2	2	2	2	21/24
Atroshi (2009)	2	2	1	2	1	1	1	2	2	2	2	2	20/24
Atroshi (2011)	2	1	2	1	1	0	2	1	2	2	2	2	18/24

Baker (2013)	2	2	0	0	0	2	2	2	2	1	1	2	16/24
Baker 2014	1	1	2	2	2	2	2	2	2	1	2	2	21/24
Bakhsh (2012)	2	2	0	2	0	1	1	1	2	2	2	2	17/24
Bessette (1998)	2	2	2	1	2	2	1	2	2	2	0	2	20/24
Boyd (2005)	2	2	2	2	0	2	2	1	2	2	1	2	20/24
Chatterjee (2009)	2	2	0	0	0	0	1	1	2	2	0	2	12/24
Cheung (2014)	2	2	2	2	2	1	2	2	2	2	2	2	23/24
Coldham (2006)	2	1	2	1	2	2	2	2	2	2	1	2	21/24
de la Llave-Rincón (2011)	2	2	2	2	1	0	2	1	2	2	2	2	20/24
Dhong (2000)	1	1	2	2	2	2	1	1	2	2	2	2	20/24
Fernandes-de-las-Penas (2009)	2	2	2	2	1	2	2	2	2	2	2	2	23/24
Gay (2003)	2	2	2	1	0	2	1	2	2	2	1	2	19/24
Greenslade (2004)	2	2	2	1	0	0	1	2	2	2	2	2	18/24
Hobby (2005)	1	1	0	2	0	1	2	2	2	2	1	2	16/24
Hsu (2015)	2	2	2	1	2	2	2	2	2	2	1	1	21/24
Jerosch-Herold (2011)	2	1	1	2	1	2	2	2	1	2	1	2	19/24
Katz (1994)	2	2	1	0	0	1	2	0	2	2	1	1	14/24
Kaye (2007)	2	1	2	2	1	2	1	2	2	2	1	2	20/24

Kotsis (2005)	1	2	0	0	0	2	2	1	2	2	1	1	14/24
Levine (1993)	2	1	1	2	0	0	2	2	2	2	1	2	17/24
Liu (2007)	1	1	1	2	0	0	2	2	1	2	1	1	14/24
Lyrén (2012)	2	1	2	2	1	1	2	1	2	2	2	1	19/24
McMillan (2009)	2	0	1	0	0	0	2	2	2	2	1	2	14/24
Ollivere (2009)	2	1	2	2	1	2	2	1	2	2	2	2	21/24
Olsen (2001)	2	0	2	1	0	2	1	0	2	1	1	2	14/24
Ozer (2013)	2	2	2	1	1	2	2	1	2	2	2	2	21/24
Özyürekoğlu (2006)	2	2	1	0	0	2	1	2	2	2	2	2	18/24
Pransky (1997)	2	1	1	2	1	0	2	1	2	2	1	2	17/24
Priganc (2003)	2	2	1	0	0	0	2	2	2	2	0	2	15/24
Sears (2010)	2	1	1	1	0	2	2	1	1	2	2	2	17/24
Smith-Forbes (2016)	2	2	2	2	2	0	0	0	2	2	2	2	18/24
Tulipan (2017)	2	2	2	2	2	2	2	2	2	2	2	2	24/24
Zyluk (2011)	1	1	1	2	0	1	1	1	2	2	0	2	14/24

[a]Law M, MacDermid J. Quality appraisal for clinical measurement studies (Appendix A). In: *Evidence-based Rehabilitation: A Guide to Practice.* 3rd ed. Thorofare, New Jersey: SLACK Inc; 2014:325-338. (Scored 0=Criterion not met; 1=Marginally meets criterion; 2=Meets criterion): (1) Comprehensive literature review to justify the research question; (2) Specific inclusion/exclusion criteria; (3) Specific hypotheses; (4) Appropriate scope of measurement properties; (5) Sample-size justification; (6) Minimal loss to follow-up; (7) Detailing the test procedures; (8) Standardization of measurement techniques; (9) Data presented for each hypothesis; (10) Appropriate statistical tests; (11) Range of analyses for each measurement property; (12) Proper presentation of the conclusions and clinical recommendations.

[b]Amirjani N, Ashworth NL, Olson JL, Morhart M, Chan KM. Discriminative validity and test-retest reliability of the Dellon-modified Moberg Pick-up Test in carpal tunnel syndrome patients. *J Peripher Nerv Syst*. 2011;16:51-58.

[c]Amirjani N, Ashworth NL, Olson JL, Morhart M, Chan KM. Validity and reliability of the Purdue Pegboard Test in carpal tunnel syndrome. *Muscle Nerve*. 2011;43:171-177.

Interventions: Assistive Technology

Study	Evaluation Criteria[a]																								
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	Total
Schmid (2015)	2	0	2	2	0	0	0	0	1	2	2	2	2	1	2	2	2	0	2	2	1	1	2	2	32/48

[a] MacDermid J.: Personal communication. Evaluation criteria (Scored 0=Criterion not met; 1=Criterion partially met; 2=Criterion met): (1) Relevant background work cited leading to a clear research question; (2) Use of comparison group; (3) Consideration of patient status more than once; (4) Prospective data collection; (5) Randomization; (6) Subjects blinded; (7) Providers blinded; (8) Independent outcomes evaluator (9) Minimal sample/selection bias; (10) Defined inclusion/exclusion criteria (11) Enrollment obtained; (12) appropriate retention; (13) Intervention applied per established principles; (14) Treatment provider biases minimized; (15) Intervention compared to appropriate comparator; (16) Primary outcome defined/appropriate; (17) Secondary outcomes considered; (18) appropriate follow up period; (19) Appropriate statistical tests performed demonstrating intervention related differences; (20)Establishment of sufficient power for identifying treatment effects; (21) Size and clinical importance of treatment group differences reported; (22) Missing data accounted for in analysis; (23) Clinical and practical significance considered when interpreting results; (24) Conclusions/clinical recommendations supported by the study objectives, analysis and results

Interventions: Orthoses

Study	Evaluation Criteria[a]																								
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	Total
Bulut (2014)	2	2	2	2	1	0	0	0	0	2	2	1	1	0	2	1	1	0	2	2	1	0	2	1	27/48
Chesterton (2018)	2	2	2	2	2	0	2	2	2	2	2	2	1	2	2	2	2	2	2	2	1	2	1	1	42/48
Courts (1995)	1	2	2	2	0	0	0	0	2	2	0	0	1	0	2	1	1	1	1	0	0	0	2	1	21/48
Ekman-Ordeberg (1987)	1	0	2	2	0	0	0	0	0	2	0	2	1	0	0	1	1	2	0	0	1	2	1	1	19/48
Gelberman (1981)	1	2	1	2	0	0	0	0	0	0	0	2	2	1	1	2	1	1	1	0	0	2	2	2	23/48
Gerritsen (2002)	2	2	2	2	2	1	2	2	2	2	0	2	2	2	2	1	2	2	2	0	2	2	2	2	42/48
Golriz (2016)	2	2	2	2	1	2	0	0	1	2	1	2	2	0	2	0	1	1	2	0	2	2	2	1	32/48
Hall (2013)	2	2	2	2	2	0	0	0	1	2	2	1	2	0	2	2	1	1	1	2	1	0	2	1	31/48
Keir (1998)	2	0	0	2	0	0	0	0	2	2	0	2	2	0	0	2	0	0	2	0	2	2	2	2	24/48
Kuo (2001)	1	0	0	2	0	0	0	0	2	1	1	0	2	0	0	2	1	0	1	0	2	2	1	1	19/48

Madjdinasab (2008)	2	2	2	2	1	2	2	0	1	2	2	2	2	0	2	2	0	2	2	0	2	0	2	2	36/48
Manente (2013)	1	0	0	2	0	0	0	0	0	1	0	2	2	0	0	1	1	0	2	0	1	1	1	2	17/48
Mishra (2006)	2	2	2	2	2	2	2	0	2	2	0	1	2	0	2	2	2	2	2	0	2	2	2	2	39/48
Özgen (2010)	2	1	2	2	0	2	2	0	0	2	0	2	2	0	2	1	1	2	2	0	2	0	2	2	31/48
Rempel (1998)	2	2	2	2	0	0	0	0	1	2	0	2	1	1	2	1	0	1	1	0	1	1	2	2	26/48
Schmid (2012)	2	2	1	2	2	0	0	2	2	2	0	2	1	2	2	2	2	0	2	0	2	1	2	1	34/48
So (2018)	1	2	2	2	2	1	0	0	2	2	2	0	1	1	2	2	2	1	2	2	1	0	2	2	34/48
Ucan (2006)	2	2	2	2	2	0	0	0	1	2	0	1	1	1	2	2	1	1	2	0	1	0	2	1	28/48
Walker (2000)	2	2	2	2	2	0	0	0	2	2	0	1	2	0	2	2	1	1	2	0	2	1	2	1	31/48
Wang (2017)	2	2	2	2	2	1	2	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	45/48
Weiss (1995)	2	1	0	1	0	0	0	0	1	1	0	2	2	0	2	2	1	0	2	0	2	2	1	1	23/48

[a]MacDermid J.: Personal communication. Evaluation criteria (Scored 0=Criterion not met; 1=Criterion partially met; 2=Criterion met): (1) Relevant background work cited leading to a clear research question; (2) Use of comparison group; (3) Consideration of patient status more than once; (4) Prospective data collection; (5) Randomization; (6) Subjects blinded; (7) Providers blinded; (8) Independent outcomes evaluator (9) Minimal sample/selection bias; (10) Defined

inclusion/exclusion criteria (11) Enrollment obtained; (12) appropriate retention; (13) Intervention applied per established principles; (14) Treatment provider biases minimized; (15) Intervention compared to appropriate comparator; (16) Primary outcome defined/appropriate; (17) Secondary outcomes considered; (18) appropriate follow up period; (19) Appropriate statistical tests performed demonstrating intervention related differences; (20)Establishment of sufficient power for identifying treatment effects; (21) Size and clinical importance of treatment group differences reported; (22) Missing data accounted for in analysis; (23) Clinical and practical significance considered when interpreting results; (24) Conclusions/clinical recommendations supported by the study objectives, analysis and results

Interventions: Biophysical Agents (Thermotherapy)

Study	Evaluation Criteria[a]																								
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	Total
Chang (2014)	2	0	1	2	2	0	2	2	2	2	2	1	2	1	2	2	2	1	2	2	2	2	2	1	39/48
Frasca (2011)	2	2	2	2	2	2	0	2	2	2	2	2	2	0	2	2	2	1	2	2	1	2	2	2	42/48
Incebiyik (2014)	2	2	2	2	2	0	2	2	1	2	0	2	2	0	2	1	2	0	2	0	2	0	1	1	32/48
Michlovitz (2004)	2	2	2	2	1	1	2	2	2	2	0	2	2	2	2	1	0	0	2	2	2	2	1	2	38/48
Ordaham (2017)	1	2	2	2	2	1	1	2	2	1	2	1	1	1	2	2	2	1	1	2	1	1	1	2	36/48

[a]MacDermid J.: Personal communication. Evaluation criteria (Scored 0=Criterion not met; 1=Criterion partially met; 2=Criterion met): (1) Relevant background work cited leading to a clear research question; (2) Use of comparison group; (3) Consideration of patient status more than once; (4) Prospective data collection; (5) Randomization; (6) Subjects blinded; (7) Providers blinded; (8) Independent outcomes evaluator (9) Minimal sample/selection bias; (10) Defined inclusion/exclusion criteria (11) Enrollment obtained; (12) appropriate retention; (13) Intervention applied per established principles; (14) Treatment provider biases minimized; (15) Intervention compared to appropriate comparator; (16) Primary outcome defined/appropriate; (17) Secondary outcomes considered; (18)

appropriate follow up period; (19) Appropriate statistical tests performed demonstrating intervention related differences; (20)Establishment of sufficient power for identifying treatment effects; (21) Size and clinical importance of treatment group differences reported; (22) Missing data accounted for in analysis; (23) Clinical and practical significance considered when interpreting results; (24) Conclusions/clinical recommendations supported by the study objectives, analysis and results

Interventions: Biophysical Agents (Electrotherapy)

Study	Evaluation Criteria[a]																								
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	Total
Koca (2014)	2	2	2	2	1	0	0	2	1	2	0	2	2	0	2	2	2	1	2	0	2	0	1	1	31/48

Interventions: Biophysical Agents (Light Agents)

Study	Evaluation Criteria[a]																								
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	Total
Raeissadat (2014)	1	2	2	2	2	0	0	1	0	2	0	2	2	0	2	1	1	1	1	0	1	0	0	0	23/48
Stasinopoulos (2005)	1	0	2	2	0	0	0	2	0	2	0	2	2	0	0	1	0	2	1	0	0	2	1	1	21/48

[a]MacDermid J.: Personal communication. Evaluation criteria (Scored 0=Criterion not met; 1=Criterion partially met; 2=Criterion met): (1) Relevant background work cited leading to a clear research question; (2) Use of comparison group; (3) Consideration of patient status more than once; (4) Prospective data collection; (5) Randomization; (6) Subjects blinded; (7) Providers blinded; (8) Independent outcomes evaluator (9) Minimal sample/selection bias; (10) Defined inclusion/exclusion criteria (11) Enrollment obtained; (12) appropriate retention; (13) Intervention applied per established principles; (14) Treatment provider biases minimized; (15) Intervention compared to appropriate comparator; (16) Primary outcome defined/appropriate; (17) Secondary outcomes considered; (18) appropriate follow up period;

(19) Appropriate statistical tests performed demonstrating intervention related differences; (20)Establishment of sufficient power for identifying treatment effects; (21) Size and clinical importance of treatment group differences reported; (22) Missing data accounted for in analysis; (23) Clinical and practical significance considered when interpreting results; (24) Conclusions/clinical recommendations supported by the study objectives, analysis and results

Interventions: Biophysical Agents (Sound Agents)

Study	Evaluation Criteria[a]																							
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	Total
Armagan (2014)	2	2	2	2	1	2	0	2	0	2	0	2	2	0	2	1	1	0	2	2	1	2	2	2	34/48
Baysal (2006)	2	2	2	2	2	0	2	2	2	2	2	1	2	0	0	0	0	2	2	0	2	0	2	0	31/48
Chang (2014)	2	2	2	2	2	0	0	2	2	2	2	1	2	0	2	2	2	2	2	1	2	0	1	2	37/48
Ebenbichler 1998	2	2	2	2	2	2	0	2	1	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	44/48
Oztas 1998	2	2	1	2	2	0	0	0	2	2	0	2	2	0	2	2	2	2	2	2	1	2	1	1	34/48

[a]MacDermid J.: Personal communication. Evaluation criteria (Scored 0=Criterion not met; 1=Criterion partially met; 2=Criterion met): (1) Relevant background work cited leading to a clear research question; (2) Use of comparison group; (3) Consideration of patient status more than once; (4) Prospective data collection; (5) Randomization; (6) Subjects blinded; (7) Providers blinded; (8) Independent outcomes evaluator (9) Minimal sample/selection bias; (10) Defined inclusion/exclusion criteria (11) Enrollment obtained; (12) appropriate retention; (13) Intervention applied per established principles; (14) Treatment provider biases minimized; (15) Intervention compared to appropriate comparator; (16) Primary outcome defined/appropriate; (17) Secondary outcomes considered; (18) appropriate follow up period; (19) Appropriate statistical tests performed demonstrating intervention related differences; (20)Establishment of sufficient power for identifying treatment effects; (21) Size and clinical importance of treatment group differences reported; (22) Missing data accounted for in analysis; (23) Clinical

and practical significance considered when interpreting results; (24) Conclusions/clinical recommendations supported by the study objectives, analysis and results

Interventions: Biophysical Agents (Transdermal Drug Delivery)

Study	Evaluation Criteria[a]																							
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	Total
Amirijani 2009	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	46/48
Bakhtiary 2013	2	1	2	2	2	1	0	2	2	2	0	2	2	0	1	2	2	1	1	0	2	2	2	2	35/48
Gökoglu 2005	1	2	2	2	1	0	0	0	2	2	0	2	2	0	1	1	1	1	2	0	2	2	2	2	30/48
Karatay 2009	1	2	2	2	1	0	0	0	0	0	0	0	1	0	2	1	1	2	1	0	1	0	1	0	18/48
Soyupek 2012	2	2	2	2	0	0	2	2	1	2	0	2	2	0	1	1	1	1	1	0	1	0	1	1	27/48
Soyupek 2012[b]	2	2	2	2	0	0	0	2	0	2	0	1	1	0	2	1	1	1	2	0	1	0	2	1	25/48
Yildiz 2011	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	1	2	2	2	2	2	2	46/48

[a]MacDermid J.: Personal communication. Evaluation criteria (Scored 0=Criterion not met; 1=Criterion partially met; 2=Criterion met): (1) Relevant background work cited leading to a clear research question; (2) Use of comparison group; (3) Consideration of patient status more than once; (4) Prospective data collection; (5) Randomization; (6) Subjects blinded; (7) Providers blinded; (8) Independent outcomes evaluator (9) Minimal sample/selection bias; (10) Defined inclusion/exclusion criteria (11) Enrollment obtained; (12) appropriate retention; (13) Intervention applied per established principles; (14) Treatment provider biases minimized; (15) Intervention compared to appropriate comparator; (16) Primary outcome defined/appropriate; (17) Secondary outcomes considered; (18) appropriate follow up period; (19) Appropriate statistical tests performed demonstrating intervention related differences; (20)Establishment of sufficient power for identifying treatment effects; (21) Size and clinical importance of treatment group differences reported; (22) Missing data accounted for in analysis; (23) Clinical and practical significance considered when interpreting results; (24) Conclusions/clinical recommendations supported by the study objectives, analysis and results

b Soyupek F, Yesildag A, Kutluhan S, et al. Determining the effectiveness of various treatment modalities in carpal tunnel syndrome by

ultrasonography and comparing ultrasonographic findings with other outcomes. *Rheumatol Int*. 2012;32:3229–3234. doi:10.1007/s00296-011-2173-7.

Interventions: Biophysical Agents (Magnet Therapy)

Study	Evaluation Criteria[a]																								
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	Total
Carter 2002	2	2	2	2	2	2	2	2	1	2	2	0	1	2	2	1	0	0	1	2	2	2	1	1	36/48
Colbert 2010	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	2	2	1	2	0	2	2	2	1	42/48

[a]MacDermid J.: Personal communication. Evaluation criteria (Scored 0=Criterion not met; 1=Criterion partially met; 2=Criterion met): (1) Relevant background work cited leading to a clear research question; (2) Use of comparison group; (3) Consideration of patient status more than once; (4) Prospective data collection; (5) Randomization; (6) Subjects blinded; (7) Providers blinded; (8) Independent outcomes evaluator (9) Minimal sample/selection bias; (10) Defined inclusion/exclusion criteria (11) Enrollment obtained; (12) appropriate retention; (13) Intervention applied per established principles; (14) Treatment provider biases minimized; (15) Intervention compared to appropriate comparator; (16) Primary outcome defined/appropriate; (17) Secondary outcomes considered; (18) appropriate follow up period; (19) Appropriate statistical tests performed demonstrating intervention related differences; (20)Establishment of sufficient power for identifying treatment effects; (21) Size and clinical importance of treatment group differences reported; (22) Missing data accounted for in analysis; (23) Clinical and practical significance considered when interpreting results; (24) Conclusions/clinical recommendations supported by the study objectives, analysis and results

Interventions: Manual Therapy and Stretching

Study	Evaluation Criteria[a]

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	Tota
Baker (2012)	2	2	2	2	2	0	2	2	1	2	0	1	2	2	2	2	2	2	2	0	2	2	1	1	38/4
Bongi (2013)	1	1	2	2	0	0	2	0	0	2	0	2	2	0	0	1	0	2	2	0	2	2	1	1	25/4
Fernández-de-las-Peñas (2015)	1	2	2	2	2	1	2	2	2	2	2	2	1	0	0	0	2	2	2	2	0	2	2	1	36/4
Fernández-de-las-Peñas (2017)	2	2	2	2	2	0	2	2	2	2	2	2	0	0	2	2	2	2	1	2	1	2	1	1	38/4
Madenci (2012)	2	2	1	2	1	0	0	0	1	2	0	2	1	0	2	2	1	1	1	1	1	1	1	1	26/4
Wolny (2018)[a]	2	2	2	2	2	2	1	2	2	2	2	0	2	1	2	2	2	1	2	2	2	0	1	2	40/4
Wolny (2018)[b]	2	2	2	2	2	2	2	2	2	2	2	1	2	1	2	2	2	2	2	2	1	2	2	1	44/4

[2a]MacDermid J.: Personal communication. Evaluation criteria (Scored 0=Criterion not met; 1=Criterion partially met; 2=Criterion met): (1) Relevant background work cited leading to a clear research question; (2) Use of comparison group; (3) Consideration of patient status more than once; (4) Prospective data collection; (5) Randomization; (6) Subjects blinded; (7) Providers blinded; (8) Independent outcomes evaluator (9) Minimal sample/selection bias; (10) Defined inclusion/exclusion criteria (11) Enrollment obtained; (12) appropriate retention; (13) Intervention applied per established principles; (14) Treatment provider biases minimized; (15) Intervention compared to appropriate comparator; (16) Primary outcome defined/appropriate; (17) Secondary outcomes considered; (18) appropriate follow up period; (19 Appropriate statistical tests performed demonstrating intervention related differences; (20)Establishment of sufficient power for identifying treatment effects; (21) Size and clinical importance of treatment group differences reported; (22) Missing data accounted for in analysis; (23) Clinical and practical significance considered when interpreting results; (24) Conclusions/clinical recommendations supported by the study objectives, analysis and results

[a] Wolny T, Linek P. Is manual therapy based on neurodynamic techniques effective in the treatment of carpal tunnel syndrome: a randomized controlled trial. Clin Rehabil

2018;10.1177/0269215518805213

[b] Wolny T, Linek P. Neurodynamic techniques versus "sham" therapy in the treatment of carpal tunnel syndrome: a randomized placebo-controlled trial. Arch Phys Med Rehabil. 2018;99:10.1016/j.apmr.2017.12.005

Systematic Reviews assessed using AMSTAR (Assessing the Methodological Quality of Systematic Reviews)[a]

Study	Section of CPG	Evaluation Criteria[b]											
		1	2	3	4	5	6	7	8	9	10	11	Total
Andersen (2011)	Risk Factors	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	9/11
Basson (2017)	Interventions	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	9/11
Geere (2007)	Outcomes measures	Yes	Yes	No	No	No	No	No	Yes	Yes	No	Yes	5/11
Hagberg (1992)	Risk Factors	Yes	No	No	Yes	No	Yes	No	No	Yes	Yes	No	5/11
Huisstede (2010)	Interventions	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	7/11
MacDermid (2004)	Differential Diagnosis	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	No	8/11
Massy-Westropp (2000)	Differential Diagnosis	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	No	6/11
Nee (2012)	Differential Diagnosis	Yes	No	Yes	Yes	No	No	Yes	Yes	No	Yes	No	6/11

O'Connor (2012)	Interventions (Ergonomic)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	10/11
Page (2012)	Interventions (Therapeutic exercise)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11/11
Page (2012)	Interventions (Orthoses)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	10/11
Palmer (2007)	Risk Factors	Yes	No	Yes	Yes	No	Yes	No	No	No	Yes	No	5/11
Rankin (2017)	Interventions	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11/11
Sakthiswarya (2017)	Risk Factors	Yes	No	Yes	Yes	No	Yes	No	No	Yes	No	Yes	6/11
van Rijn (2003)	Risk Factors	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	9/11

[a]Shea *et al. BMC Medical Research Methodology.* 2007;7:10. doi:10.1186/1471-2288-7-10. (Evaluation criteria: Yes; No; Can't answer; Not applicable) (1) a priori design provided; (2) Duplicate study selection and extraction; (3) Comprehensive literature search performed; (4) Status of publication used as an inclusion criterion; (5) List of studies (included and excluded) provided; (6) Characteristics of included studies provided; (7) Scientific quality of included studies assessed and documented; (8) Scientific quality of included studies used appropriately in formulating conclusions; (9) Methods used to combine the findings of studies was appropriate; (10) Likelihood of publication bias assessed; (11) Conflict of interest included

APPENDIX E. ARTICLES USED IN DEVELOPING RECOMMENDATIONS
Diagnosis

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Interventions: Orthoses

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Interventions: Biophysical Agents (Thermotherapy)

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Interventions: Biophysical Agents (Transdermal Drug Delivery)

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Interventions: Biophysical Agents (Magnet Therapy)

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Interventions: Manual Therapy and Stretching

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APPENDIX F. Levels of Evidence Table*

	Intervention/ Prevention	**Pathoanatomic/Risk/ Clinical Course/ Prognosis/Differential Diagnosis**	**Diagnosis/Diagnostic Accuracy**	**Prevalence of Condition/ Disorder)**	**Exam/ Outcomes**
I	Systematic Review of High Quality Randomized Clinical Trials (RCTs) High Quality RCT[a]	Systematic Review of Prospective Cohort Studies High Quality Prospective Cohort Study[b]	Systematic Review of High Quality Diagnostic Studies High Quality Diagnostic Study[c] with validation	Systematic Review High Quality Cross-Sectional Studies High Quality Cross-Sectional Study[d]	Systematic Review of Prospective Cohort Studies High Quality Prospective Cohort Study
II	Systematic Review of High Quality Cohort Studies High Quality Cohort Study[b] Outcomes Study or Ecological Study Lower quality RCT[e]	Systematic Review of Retrospective Cohort Study Lower Quality Prospective Cohort study High Quality Retrospective Cohort Study Consecutive Cohort Outcomes Study or Ecological Study	Systematic review of Exploratory Diagnostic Studies or Consecutive Cohort studies High Quality Exploratory Diagnostic Studies Consecutive Retrospective Cohort	Systematic review of studies that allows relevant estimate Lower Quality Cross-Sectional Study	Systematic Review of Lower Quality Prospective Cohort Studies Lower Quality Prospective Cohort Study
III	Systematic Reviews of Case-control Studies High Quality Case-Control Study Lower Quality Cohort Study	Lower Quality Retrospective Cohort Study High Quality Cross Sectional Case-Control Study	Lower Quality Exploratory Diagnostic Studies Non-Consecutive Retrospective Cohort	Local Non-Random Study	High Quality Cross-Sectional Study
IV	Case-Series	Case-Series	Case-Control Study		Lower Quality Cross-Sectional Study
V	Expert Opinion	Expert Opinion	Expert Opinion	Expert Opinion	Expert Opinion

*Adapted from Oxford Centre for Evidence-based Medicine Levels of Evidence 2009. Bob Phillips, Dave Sackett, Doug Badenoch, Sharon Strauss, Brian Haynes, Martin Dawes, since 1998. Updated by Jeremy Howick March 2009. See also Procedures for Assigning Levels of Evidence.

[a]High quality includes RCT>80% follow-up; blinding; appropriate randomization procedures.

[b]High quality cohort study includes >80% follow-up.

[c]High quality diagnostic study includes consistently applied reference standard and blinding.

[d]High quality prevalence study is a cross-sectional study that uses a local and current random sample or censuses.

[e] Weaker diagnostic criteria and reference standards, improper randomization, no blinding, <80% follow-up may add threats to bias and validity

APPENDIX G. Procedures for Assigning Levels of Evidence

1. Level of evidence is assigned based on the study design using the Levels of Evidence Table, assuming High Quality (eg, for intervention randomized clinical trial (RCT) starts at Level I).
2. Study quality is assessed using the critical appraisal tool, and the study is assigned 1 of 4 overall Quality Ratings based on the critical appraisal results.
3. Level of Evidence assignment is adjusted based on the overall quality rating:
    - **High Quality** (high confidence in the estimate/results) – ***study remains at assigned level of evidence*** (eg, if the RCT is rated high quality, its final assignment is Level I). High quality should include:
        - RCT with >80% follow-up; blinding; appropriate randomization procedures.
        - Cohort study includes >80% follow-up.
        - Diagnostic study includes consistently applied reference standard and blinding.
        - Prevalence study is a cross-sectional study that uses a local and current random sample or censuses.

    - **Acceptable Quality** (the study does not meet requirements for high quality, weaknesses limit the confidence in the accuracy of the estimate) – ***downgrade 1 level***
        - Based on critical appraisal results
    - **Low Quality**: the study has significant limitations that substantially limit confidence in the estimate – ***downgrade 2 levels***
        - Based on critical appraisal results
    - **Unacceptable Quality** – serious limitations - ***exclude from consideration in the guideline.***
        - Based on critical appraisal results