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SUMMARY WITH CRITICAL APPRAISAL

Orthotic Bracing or Splinting of Upper Extremities in Patients with Chronic, Non-Cancer Pain: A Review of Clinical Effectiveness

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Abbreviations

AE	Adverse event
aMD	Adjusted mean difference
AMSTAR 2	A Measurement Tool to Assess systematic Reviews - version 2
AUSCAN	Australian/Canadian Hand Osteoarthritis Index
BCTQ	Boston Carpal Tunnel Questionnaire
CCTs	Controlled clinical trials
CI	Confidence interval
CMC	Carpometacarpal joint
CTS	Carpal tunnel syndrome
DASH	Disabilities of the Arm, Shoulder and Hand
DIP	Distal interphalangeal joint
FSS	Functional status scale
GRADE	Grading of Recommendations Assessment, Development and Evaluation
MD	Mean difference
MHQ	Michigan Hand Outcomes Questionnaire
NPRS	NPRS
OA	Osteoarthritis
RCT	randomized controlled trial
RoBANS	Risk of Bias for Nonrandomized Studies
SD	Standard deviation
SIGN	Scottish Intercollegiate Guidelines Network
SSS	Symptom severity scale
TMC	Trapeziometacarpal joint
VAS	Visual analogue scale

Context and Policy Issues

Upper extremity pain can significantly reduce an individual's ability to complete their activities of daily living.[1] Frequently used pharmacological treatments for upper extremity pain include non-steroidal anti-inflammatory drugs, acetaminophen, topical capsaicin, and topical salicylates as well as less conventional drugs such as pregabalin and duloxetine.[2] Interventions involving multidisciplinary teams using a multimodal approach combining splints with other components, such as education or exercise delivered by occupational therapists, have been reported in the literature to be more effective at managing pain than single isolated interventions.[3,4]

Splint refers to a rigid or flexible appliance for fixation of displaced or movable parts.[5] They are used to stabilize injuries by decreasing movement and providing support, to prevent further damage, as well as to alleviate pain and edema, and promote soft-tissue and bone healing.[6] Splints are frequently applied to immobilize an extremity in advance of a surgical procedure or as a temporary measure while awaiting orthopedic consultation.[6]

Although splinting is commonly used in clinical practice with the intent to reduce hand and wrist pain, improve hand function, and reduce or prevent deformity and soft tissue contractures, the evidence of efficacy is unclear.[7] Therefore, the objective of this report is to review and summarize evidence regarding the clinical effectiveness of orthotic bracing and splinting of the upper extremities in patients with chronic, non-cancer pain.

Research Question

What is the clinical effectiveness of orthotic bracing and splinting of the upper extremities in patients with chronic, non-cancer pain?

Key Findings

Evidence of limited quality from the two included systematic reviews suggested that compared to usual care or no intervention, splint use significantly reduced pain and improved functional performance in patients with osteoarthritis involving the thumb base (rhizarthrosis), carpometacarpal joints, or the distal interphalangeal joint in the long-term (13 to 52 weeks) but not in the short term.

Evidence of limited quality from four prospective, uncontrolled, before-and-after studies suggested that compared to baseline, the use of splints for four to six weeks resulted in statistically significant reduction in pain, improvement in functional performance, as well as range in motion, pinch strength, and hand strength in in patients with osteoarthritis involving the distal interphalangeal joint, and trapeziometacarpal joints, or those diagnosed with tennis elbow or carpal tunnel syndrome.

Evidence from the two included randomized controlled trials (RCTs) indicated that a single local injection of 20 mg methylprednisolone acetate was statistically significantly more effective than night splitting for reducing pain intensity and improved figure dexterity in patients with carpal tunnel syndrome after four to six weeks of treatment. However, the findings from these RCTs on functional performance were inconclusive as one reported a statistically significantly greater improvement in favor of the steroid injection, whereas the other did not find a significant between group difference.

Sources of uncertainty in the current report included a lack of definition of ‘‘usual care,’’ and a significant overlap of primary studies, all of which had high risk of bias between the two included systematic reviews. Also, the comparator data used in meta-analysis were from usual care or no intervention without reporting separate results for either of them compared to splint. Given that lack of treatment might not result in improved outcomes, it is unclear if splints might perform equally well in comparison with usual care alone as they did in analyses that considered data from usual care or no treatment together as comparator group.

Fundamental limitations of the primary studies included in this report were the open-label design of all which disposes them to biases and the fact that four of them were prospective, uncontrolled, before-and-after studies with inherently higher likelihood of systemic biases due to lack of the risk-diminishing property of randomization. Also, the before-and-after studies investigated different kinds of splints, with variations in design and materials used in construction, custom-made devices, and splints fabricated by patients for self-use. Thus, it was unclear if the finding of these studies could be replicated using generic splints.

There were no studies identified that compared splints to pharmacological interventions for pain relief such as non-steroidal anti-inflammatory drugs, acetaminophen, topical capsaicin, and topical salicylates, as well as less conventional medications such as pregabalin and duloxetine. Furthermore, none of the studies included in this report provided outcomes on health-related quality of life, disability level, or global impression of recovery after treatment with any of the studied interventions.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources, including PubMed, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were upper extremity pain and splitting/bracing. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 01, 2015, and January 27, 2020.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed, and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults living with chronic non-cancer pain, excluding pregnant patients
Intervention	Orthotic braces and splinting of upper extremities (e.g., hand, wrist, elbow, shoulder)
Comparator	Pharmacological interventions No treatment (no splinting) Usual care (if usual care is pharmacological interventions only) [a]
Outcomes	Clinical effectiveness (pain reduction, functional performance, quality of life, disability level, safety, global impression of recovery, adverse events)
Study Designs	HTA/Systematic Reviews/Meta-Analyses, Randomized Controlled Trials, Non-Randomized Studies

[a] Systematic reviews with "usual care" comparators, when not otherwise specified, were included. Descriptions of pharmacological interventions in selected studies were provided when available.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1; they were duplicate publications or were published before 2015.

Critical Appraisal of Individual Studies

One reviewer critically appraised the studies included in this report using different appraisal tools to match the various study designs as follows: version two of A Measurement Tool to Assess systematic Reviews (AMSTAR 2)[8] for systematic reviews, (SIGN) Methodology Checklist 2: Controlled Trials[9] for randomized controlled trials, and the Risk of Bias for Nonrandomized Studies (RoBANS)[10] for non-randomized studies. Summary scores were not calculated for the included studies; instead, the strengths and limitations of each included study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 420 citations were identified in the literature search. Following screening of titles and abstracts, 396 citations were excluded, and 24 potentially relevant reports from the electronic search were retrieved for full-text review. A grey literature search did not identify any potentially relevant publications. Of these 24 potentially relevant articles, 16 papers were excluded for various reasons. Thus, eight publications – two systematic reviews,[2,11] two randomized controlled trials (RCTs),[12,13] and four prospective, uncontrolled, before-and-after studies[14-17] – met the inclusion criteria and were included in this report.

Appendix 1 presents the PRISMA[18] flowchart of the study selection.

Summary of Study Characteristics

Additional details regarding the characteristics of included publications are provided in Appendix 2.

Study Design

Two systematic reviews,[2,11] two randomized controlled trials (RCTs),[12,13] and four prospective, uncontrolled before-and-after studies[14-17] were included in this report.

Systematic reviews

One systematic review was authored by Meireles et al. and published in 2019.[11] Systematic searches for relevant literature for this systematic review were performed in multiple databases from inception until December 2017 with no language restriction.[11] A total 14 randomized controlled trials (RCTs) were included in the systematic review, of which seven RCTs on orthoses met the criteria of interest to this Rapid Response review. The remaining seven did not meet the criteria because at least one study arm had a combination of interventions, or they compared different types of splints to each other and no comparator of interest to this Rapid Response review.

The second included systematic review was authored by Kroon et al. and published in 2018.[2] Systematic searches for relevant literature for that systematic review were performed in multiple databases from inception up to June 2017.[2] A total of 127 RCTs and non-randomized controlled clinical trials (CCTs) were included in the systematic review,[2] including 14 studies that investigated and reported outcomes after splint use. Of these 14 studies on splint, five RCTs and one CCT met the criterial of interest to this Rapid Response review. The remaining eight did not meet the criteria because at least one study arm had a combination of interventions or they compared different types of splints to each other and had no comparator of interest to this Rapid Response review.

Both systematic reviews[2,11] combined data from studies that evaluated splint use meeting the inclusion criteria of this Rapid Response report in meta-analyses to determine effect estimates of various outcomes of interest. There was significant overlap in the primary studies of the two of the systematic reviews,[2,11] with five RCTs of the six relevant studies from one systematic review[2] counted among the seven relevant RCTs in the other systematic review.[11] Details regarding the primary study overlap among included systematic reviews are provided in Appendix 5.

Randomized controlled trials

One RCT (by Chesterton et al.)[12] published in 2018 was an open-label, multi-site study conducted in 25 primary and community musculoskeletal clinics and services.[12] The second RCT (by So et al.),[13] also published in 2018, was a single-center open-label study conducted in the general medical unit of a local hospital.[13]

Non-randomized studies

All the four prospective, uncontrolled before-and-after studies[14-17] were single-center, open-label studies. One of them was conducted by Tada et al.[14] and published 2018. One each of the remaining three, all published in 2016, was conducted by Maddali-Bongi et al.,[15] Najafi et al.,[16] and Weng et al.[17] The study by Maddali-Bongi et al.[15] was conducted in a local clinical setting, whereas the remaining three studies[14,16,17] were conducted at university hospitals.

Country of Origin

Systematic Reviews

The systematic reviews by Meireles et al.[11] and Kroon et al.[2] were conducted in Brazil and the Netherlands, respectively.

Primary studies

The RCT by Chesterton et al.[12] was conducted in the United Kingdom, whereas the RCT by So et al.[13] and the prospective, uncontrolled, before-and-after cohort study by Weng et al.[17] were conducted in China. One each of the three other prospective, uncontrolled, before-and-after studies was conducted in Japan,[14] Italy,[15] and Iran.[16]

Patient Population

Systematic Reviews

In the systematic review by Meireles et al.,[11] the seven included RCTs of interest to this report had a total of 357 patients with thumb base osteoarthritis (rhizarthrosis). No information was provided about the patients' characteristics or study settings.[11] The six studies of interest in the systematic review by Kroon et al.[2] involved a total of 315 patients with hand osteoarthritis (OA) involving first carpometacarpal joint (CMC), distal interphalangeal joint (DIP), or thumb pain. Most (≥ 67%) of the patients in the six relevant primary studies were women, and the mean age of the study population varied from 50.2 to 65.1 years. No information was provided about the study settings.[2]

Randomized controlled trials

The two RCTs[12,13] were conducted in adult patients (18 years or older) with carpal tunnel syndrome (CTS). Chesterton et al.[12] enrolled a total of 234 patients, whereas the RCT by So et al.[13] involved 50 patients. For the RCT by Chesterton et al.,[12] the mean ages of the patients in the splint and corticosteroid groups were 52.2 years and 52.6 years, respectively; and 69% and 63% of the study population was female, respectively. In the RCT by So et al.,[13] the mean ages of patients in the splint and corticosteroid groups were 57.28 years and 57.31 years, respectively; and 88% and 84% of the study population was female, respectively.

Non-randomized studies

Tada et al., 2018[14] enrolled a total of 30 patients with painful OA of the DIP, whereas a total of 50 patients with OA of the trapeziometacarpal (TMC) joint were involved in the study by Maddali-Bongi et al.[15] The study by Najafi et al.[16] enrolled a total of 15 patients with tennis elbow and Weng et al.[17] included a total of 41 patients with CTS. The mean age across the studies varied from 43 years to 72 years, and the study population comprised mostly females (67% to 93%).

Interventions and Comparators

Systematic Reviews

In the systematic reviews by Meireles et al.[11] and that by Kroon et al. 2019,[2] orthosis (splint) was the index intervention. Direction provided for using the splints included wearing them to perform activities of daily living, use as needed, and wearing at night. Although each of the systematic reviews[2,11] investigated a variety of comparators to splint, the comparison of interest to this Rapid Response report were "no interventions" and "usual care." Usual care was not defined in either of the systematic reviews.[2,11]

Randomized controlled trials

In the two RCTs,[12,13] patients were randomly assigned to be treated with a night splint or corticosteroid injection. Participants randomized to receive splints were instructed to wear them at night for six weeks in the RCT by Chesterton et al.[12] and one month in the study by So et al.[13] In both RCTs,[12,13] patients assigned to the corticosteroid group received a single dose of 20 mg methylprednisolone acetate by injection into the carpal tunnel.

Non-randomized studies

Patients in all four prospective, uncontrolled, before-and-after studies[14-17] were treated with splints. However, the type of splint varied across the studies. In the study by Tada et al.,[14] patients received a tin ring splint to wear when in pain for up to six months, whereas patients in the study by Maddali-Bongi et al.[15] were given a custom-made 'butterfly' splint made of thermoplastic material to be worn 16 hours per day (during waking hours, not at night) for 30 days. In the study by Najafi et al.,[16] all patients were given a spiral splint and asked to wear for 12 hour a day for four weeks when performing activities of daily living. In the study by Weng et al.,[17] all patients were instructed to make splints out of stereoplasm, which they were asked to wear at bedtime for three months to immobilize the wrist in the neutral posture.

Outcomes

Systematic Reviews

Common outcomes of interest reported in the two included systematic reviews were pain and function. Pain was commonly assessed using visual analogue scale (VAS) or numerical pain rating scale (NPRS) of various ranges, with higher scores indicating greater pain on each scale. Instruments used to evaluate function in the primary studies of both systematic reviews[2,11] included the 0 to 90 scale Australian/Canadian Hand Osteoarthritis Index (AUSCAN; higher scores indicating better function), the Disabilities of the Arm, Shoulder and Hand questionnaire (DASH; 0 to 100 scale; higher scores indicating worse function), Michigan Hand Outcomes Questionnaire (MHQ; 0 to 100 scale; higher scores implied better function). In addition to pain and function, Meireles et al.[11] reported on pinch strength measured with a pinch gauge, whereas Kroon et al.[2] reported on grip strength but

did not specify the tool for measurement. For the two systematic reviews, the duration of the follow-up in the relevant included primary studies varied between two weeks and 12 months.

Randomized controlled trials

The two RCTs[12,13] evaluated changes in the overall scores for symptom severity and hand function using the Boston Carpal Tunnel Questionnaire (BCTQ). The BCTQ is a disease-specific questionnaire comprising two subscales: symptom severity scale (SSS) with 11 items and functional status scale (FSS) with eight items. It is used to assess patients' condition in a typical 24-hour period in the last two weeks after completing the baseline assessment or completing the questionnaire in a previous follow-up evaluation. In addition to the overall score, both RCTs[12,13] also reported scores for FSS and SSS subscales. In addition to the BCTQ scores, Chesterton et al.[12] assessed the hand–wrist pain intensity (no details provided) and adverse events (AE), whereas So et al. evaluated figure dexterity using the validated nine-hole peg test.[13]

Non-randomized studies

Three prospective, uncontrolled, before-and-after studies[14-16] performed assessment of pain and function outcomes. Pain endpoints were evaluated on a NPRS[14,15] or VAS,[16] with higher scores signifying worse pain on either scale. Improvement in function was measured using Hand 20 functional assessment criteria of the upper extremities,[14] the Dreiser scale,[15] or the DASH score.[16] The Hand 20 is a 20-item instrument used to assess the overall function of the upper extremity in the last week, with the score ranging from 0 (no issues) to 100 points (worst possible case). The Dreiser scale is a 10-item questionnaire used to evaluate the hand ability and pain in the usual tasks of daily life.[15] The scoring is on a four-level scale for each item (i.e., from 0 = no difficulty to 3 = inability) for a total score ranging 0 to 30, with higher scores trending with higher disability.[15] The DASH is used to assess physical function (2 items), disease symptoms (6 items), and social aspects (3 items), and it has two optional modules (4 items) for workers and athletes.[16] Higher DASH scores denote worse function.[16] Other outcomes that were assessed by these three prospective, uncontrolled, before-and-after studies[14-16] included range of motion,[14] hand strength,[15] pinch strength,[15] and grip strength.[14-16] Changes in hand strength and grip strength were measured using Jamar dynamometer,[15,16] and pinch strength was assessed with pinch gauge.[15]

The fourth prospective, uncontrolled, before-and-after study[17] evaluated patients' functional status and symptoms severity using FSS and SSS, respectively.

Summary of Critical Appraisal

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

Systematic Reviews

The two systematic reviews[2,11] included in this report stated their objectives and defined populations, interventions, comparators, and outcomes. However, there was no indication that any of the systematic reviews[2,11] were based on a protocol written beforehand and with independent verification. All their primary studies were identified from comprehensive literature searches. Although the authors did not provide a rationale for selecting the types of study designs to include in the reviews, the eligibility strategies seemed reasonable given

that enough RCTs[2,11] and non-randomized clinical controlled trials[2] were available to answer the questions of interest, without the need to include study designs of lower quality.

In one of the systematic reviews,[11] two reviewers independently selected studies, conducted quality assessment, and extracted data, with arrangement to resolve conflicts through a third researcher. However, in the second systematic review,[2] one reviewer determined the eligibility of studies for inclusion and the same individual performed data extraction. Thus, there was no measure in place to mitigate the risk of study selection bias or ensure independent verification of extracted data.

Each of the systematic reviews[2,11] described the characteristics of primary included studies in tabular form. However, neither provided a list of excluded studies along with the reasons for excluding them. The methodological quality of the primary studies included in systematic reviews[2,11] were evaluated using Cochrane Collaboration's Risk of Bias tool[2,11,19,20] and the Physiotherapy Evidence Database (PEDro)[11] scale, both of which are well-known, widely-used assessment tools for such purposes. One systematic review[11,21] rated the quality of the evidence using Grading of Recommendations Assessment, Development and Evaluation (GRADE) method.

In one systematic review,[11] heterogeneity was assessed using the I^2 statistical test, and models were selected to combine the results from the individual studies in meta-analysis depending on the level of heterogeneity. Although the authors of the other systematic review[2] reported that there was heterogeneity in many of the included studies, the method for making that determination was not described, and a justification was not provided for the choice of statistical model used to combine data from the individual included studies. Neither of the systematic reviews[2,11] assessed for publication bias in their primary studies to evaluate any potential impact of small samples, methodological limitations in trials, or heterogeneity in interventions or populations on the reported outcomes. Also, the sources of funding for the included studies was not reported in either of the systematic reviews.[2] However, each systematic review considered heterogeneity and the general risk of bias in their primary studies in the discussion and interpretation of their results.[2,11]

Randomized controlled trials

Both RCTs[12,13] included in this report stated their study objectives and randomly assigned the participants to treatment groups. However, each RCT had an open-label design study. Thus, the studies had inherently high risk of bias due to lack of blinding and difficulty in achieving adequate concealment, especially considering the treatment under investigation. Even so, one of the RCT[12] reported that the allocation sequence was not available to research team members, and the treatment group allocation was concealed during the analyses. One RCT[12] enrolled patients from 25 primary and community musculoskeletal clinics and services whereas the other RCT[13] recruited consecutive patients attending the general medical unit of a local hospital. Therefore, the study participants in the RCTs[12,13] were likely to be a representative sample from the general patient population presenting with the targeted upper extremity conditions,[12,13] and generalizability was enhanced. In each of the RCTs,[12,13] the demographic and disease condition characteristics at baseline were similar across the treatment and control groups, with the interventions under investigation being the only inter-group difference, to which any observed significant difference in outcomes could be rightly attributed. In both RCTs,[12,13] all relevant results were measured using standard validated and reliable instruments, including the Boston Carpal Tunnel Questionnaire (BCTQ) which is specific to patients with carpal tunnel syndrome who constituted the study population in the two studies. Each of the studies[12,13]

performed calculations to determine a sample size that ensured the study was sufficiently powered to detect a true difference between the two intervention groups. In one RCT,[13] the primary analysis was based on the intention-to-treat population, and the percentage of missing data was low (≤5%) and unlikely to affect the reported results. The missing data was handled through multiple imputation, with the results compared in a sensitivity analysis with findings based on data from patients who completed the study without missing data.[12] In the other RCT,[13] all the randomized patients completed the study procedures and there was no report of missing data. The authors in both RCTs[12,13] declared that they had no competing interest. Thus, no conflict could potentially impact the design and conduct of the study, data collection, analysis, and interpretation of the results.

Non-randomized studies

The lack of the risk-diminishing property of randomization to the intervention or a comparator group in the four included prospective, uncontrolled, before-and-after studies[14-17] indicate an inherent likelihood of systemic biases. Even so, the risk of bias due to selection of study participant is low in all the studies, given that the study population in each study remained the same for comparisons before and after exposure to the intervention under study. Also, the risk of reporting bias due to selective outcome reporting was low in all the four studies[14-17] because most of the expected key outcomes based on the stated study objectives were reported.

All four included prospective, uncontrolled, before-and-after studies[14-17]did not mention potential confounding factors, such as natural course of disease (e.g., primary exacerbations, transient relief from symptoms) or differences in lifestyle that may influence outcomes, and no confounder was considered during analysis or design. Therefore, there is a high potential for risk of selection bias due to inappropriate confounder confirmation and consideration. Also, all four studies[14-17] had open-label design, with no indication of any measure taken to ensure that outcome assessors were blinded to patients' treatment. Thus, a high potential existed for confirmation bias due to inappropriate blinding of assessors.

In three of the studies,[14-16] data were collected prospectively from the same consecutively recruited patients at baseline and follow-up assessments, thus minimizing the risk of target group selection bias due to selective application of the intervention or due to using only participants with good outcomes in the selection process, as could potentially happen if data was collected retrospectively. However, in one other study,[17] which also collected data prospectively from the same consecutively recruited patients at baseline and follow-up assessments, the risk of selection bias due to inappropriate intervention could not be ruled out. The reason for the uncertainty was that each patient in that study was instructed to make and use their own splint, and the resulting variations in the devices used by the individual patients could have potentially influenced the reported outcomes.

Three of the studies[14-16] used validated instruments to assess outcomes at multiple follow-up timepoints, thus lowering the risk of confirmation bias due to inappropriate outcome assessment methods. However, one other study[17] did not specify the instrument used in the assessment of outcomes. Thus, the risk of confirmation bias due to inappropriate outcome assessment methods could not be ruled out.

In two of the studies,[15,16] the risk of performance bias due to inappropriate intervention or inappropriate exposure measurement was low because the frequency of applying the splint was standardized, and compliance was high. Also, the risk of attrition bias due to improper handling of incomplete data was low in both studies,[15,16] as all enrolled patients were

retained over the entire duration of the study, and they continued to use their splint until the end of the without missing data. However, in two other studies,[14,17] there was a potentially high risk of performance bias due to differences in exposure resulting from a lack of standardized frequency of applying the splints[14,17] or significant differences in the splints[17] used by patients. The risk of attrition bias due to inappropriate handling of incomplete data was unclear in each of the two studies[14,17] because the authors did not provide information about compliance, dropout rate, or missing data.

Summary of Findings

Appendix 4 presents a table of the main study findings and authors' conclusions.

Clinical Effectiveness of orthotic bracing and splinting of the upper extremities in patients with chronic, non-cancer pain

Pain reduction

Two systematic reviews,[2,11] one RCT,[12] and three prospective, uncontrolled, before-and-after studies[14-16] reported pain outcomes after splint use.

Splint versus usual care or no intervention

Two systematic reviews,[2,11] reported pain relief outcomes comparing the use of splint to usual care (not defined) or no intervention. Based on meta-analysis of data from two primary studies (n = 141 patients with thumb base OA), Meireles et al.[11] reported no significant difference in pain between splint and usual care or no intervention in the short-term (not defined). Similarly, Kroon et al.[2] found that in patients with hand OA (n = 221, from four studies), the use of thumb splint did not result in a statistically significantly greater reduction in pain than usual care or no intervention, after four to eight weeks of treatment.

However, in a meta-analysis of data from three primary studies (n = 203), Meireles et al.[11] found that over the long-term (not defined) the use of splints resulted in a statistically significantly greater reduction in pain than usual care or no intervention with effect estimate of −0.52 (95% CI: −0.94 to −0.11; P = 0.01). Consistent with that finding, Kroon et al.[2] found from analysis of data from two primary studies (n = 137) that pain reduction with thumb splint was significantly better than usual care or no intervention after 13 to 52 weeks of treatment, with a mean difference (MD) of −17.4 (95% CI: −25.6 to − 9.2, P value not reported).

Splint versus steroid injection

One RCT[12] found that in patients with mild to moderate carpal tunnel syndrome (CTS), a single dose of 20 mg methylprednisolone acetate administered by injection after randomization reduced hand-wrist pain intensity statistically significantly more at six weeks follow-up evaluation than nightly use of splint for six weeks, with an adjusted mean difference (aMD) of –0.97 (95% CI: –1·64 to –0·30; P = 0·0049).

Splint use in studies comparing outcomes in the same patients without comparator groups

Three prospective, uncontrolled, before-and-after studies[14-16] consistently reported that using splint for a month reduced pain associated with OA of the hand[14,15] or tennis elbow.[16]

In the study by Tada et al.,[14] 25 (83.3%) patients with painful OA of the DIP reported pain relief after one month of splint use, with lessening symptoms commonly reported by the 10th day after treatment. However, five (16.7%) patients had no perceptible change in pain.

The mean pain score on a 0 to 100 NPRS decreased significantly from 58.4 at baseline to 33.1 (P < 0.001) after one month of splint use. Maddali-Bongi et al.[15] found similar reduction on a 0 to10 NPRS among patients with trapeziometacarpal OA for whom the mean pain score reduced from 5.99 at baseline to 2.61 (P < 0.0001) after one month of splint use. The assessment at the 12-month follow-up showed that the pain reduction remained significant (P < 0.0001) relative to the baseline, with mean score of 3.22. Najafi et al.[16] assessed pain outcomes in patients with tennis elbow with 0 to 10 VAS and found that splint use resulted in a statistically significant level of pain relief as indicated by a reduction in mean score from 8.0 at baseline to 2.6 (P < 0.001) after four weeks.

Functional performance

Two systematic reviews,[2,11] two RCTs,[12,13] and four prospective, uncontrolled, before-and-after studies[14-17] reported outcomes about functional improvement after splint use.

Splint versus usual care or no intervention

Two systematic reviews,[2,11] reported outcomes about changes in function comparing the use of splint to usual care or no intervention. Based on meta-analysis of data from two primary studies (n = 141 patients with thumb base OA), Meireles et al.[11] reported no significant difference in improvement in function between splint and usual care or no intervention in the short-term. Similarly, a meta-analysis by Kroon et al.[2] found that in patients with hand OA (n = 144, from three primary studies), the use of thumb splint did not result in a statistically significantly greater improvement in function than usual care or no intervention, after four to eight weeks of treatment. One primary RCT (n = 26) in the same systematic review[2] also reported that after 12 weeks of treatment, improvement in function in patients with DIP OA was not statistically significantly better than who received usual care or no intervention.

However, a meta-analysis of data from three primary studies (n = 203), Meireles et al.[11] found that over the long-term the use of splints resulted in a statistically significantly greater improvement in function than usual care or no intervention with an effect estimate of -0.44 (range: -0.72 to -0.15; P = 0.002). Similarly, one primary RCT (n=112) included in the systematic review by Kroon et al.[2] reported that after 52 weeks of treatment, improvement in functional performance was significantly better with thumb splinting than with usual care (MD −6.3; 95% CI −10.9 to −1.7; P value not reported).

Splint versus steroid injection

Two RCTs[12,13] reported inconsistent functional status and symptom severity outcomes based on BCTQ scores. The RCT by Chesterton et al.[12] found at the sixth-week follow-up evaluation that in patients with mild to moderate CTS, statistically significantly greater improvement in overall mean BCTQ score occurred with a single injection of 20 mg methylprednisolone acetate administered after randomization than nightly use of splint for six weeks, with an adjusted mean difference (aMD) of –0.32 (95% CI: –0.53 to –0.17; P = 0.0001). The BCTQ subscales scores were consistent with the overall BCTQ results, with corticosteroid injection showing significantly better improvements than night splint on both the functional limitation and symptom severity subscale at the six weeks assessment.

However, the RCT by So et al.[13] found no significant difference between the local steroid injection and splinting with regards to the overall BCTQ or its SSS and FSS subscales after four weeks treatment. It was unclear whether the difference in the duration of the studies

could explain why one RCT,[12] and not the other,[13] found a statistically significant inter-group difference in the BCTQ scores.

Splint use in studies comparing outcomes in the same patients without comparator groups

Four prospective, uncontrolled, before-and-after studies[14-17] consistently reported that splinting improved functional performance in patients with OA of the hand[14,15] or tennis elbow.[16,17]

In the study by Tada et al.,[14] functional assessment in patients with painful OA of the DIP showed a significant improvement from a mean Hand 20 score of 35.0 baseline to 20.2 (P = 0.001) after six months treatment. Using the Dreiser scale for assessments, Maddali-Bongi et al.[15] showed that hand function and ability in patients with TMC OA improved significantly from baseline after using splint, as indicated by a reduction in mean scores from 6.8 to 4.42 (P = 0.001) at the one-month follow-up assessment. Najafi et al.[16] found similar improvement in functional performance indicated by a reduction in the mean DASH score from 20.74 at baseline to 8.99 at the four-week assessment (P < 0.001). Also, the study by Weng et al.[17] reported that patients with tennis elbow, instructed to wear the splint when they felt pain, had statistically significant improvements in function from baseline represented by reductions in both the functional status score (1.77 to 1.55; P < 0.001) and symptom severity score (1.53 to 1.40; P < 0.001). The instrument used for the assessment was not identified in the study.

Pinch Strength

One systematic review[11] and one prospective, uncontrolled, before-and-after study[15] reported pinch strength outcomes after splint use.

Splint versus usual care or no intervention

From analysis of data from two primary studies (n = 142), the systematic review by Meireles et al.[11] found no significant difference in pinch strength between splint and usual care or no intervention in the short-term or long-term.

Splint use in studies comparing outcomes in the same patients without comparator groups

One prospective, uncontrolled, before-and-after study by Maddali-Bongi et a.[15] reported that in patients with TMC joint OA, pinch strength significantly improved from an overall mean of 4.52 kg on a pinch gauge at baseline scores to 5.17 kg at the one-month follow-up assessment (P < 0.0001).

Grip Strength,

One systematic review[2] and one prospective, uncontrolled, before-and-after study[16] reported grip strength outcomes after splint use.

Splint versus usual care or no intervention

In the systematic review by Kroon et al.,[2] analysis of data from two primary studies (n = 95) found that improvement in grip strength was not statistically significantly different for patients who used thumb splits compared to usual care or no intervention.

Splint use in studies comparing outcomes in the same patients without comparator groups

One prospective, uncontrolled, before-and-after study by Najafi et al.[16] reported that in patients with tennis elbow, grip strength significantly increased from an overall mean 7.87 kg at baseline scores to 8.99 kg, (P < 0.001) after 4 weeks of using splint.

Hand strength

Splint use in studies comparing outcomes in the same patients without comparator groups

One prospective, uncontrolled, before-and-after study by Maddali-Bongi et al.[15] reported that assessment of hand strength in patients with TMC joint OA showed significant increase in mean score hand muscle strength on a dynamometer from 37.46 at baseline scores to 49.64 after one month of splint use ($P < 0.0001$)

Finger Dexterity

Splint versus steroid injection

One RCT by So et al.[13] found that at the four-week follow-up assessment, patients with CTS treated with local steroid injection after randomization had significant improvement in figure dexterity as indicated by the change in the median nine-hole peg test score of –2.56 (range: –9.47 to 7.73; $P = 0.038$), whereas improvement in those who used splint during the same period did not reach the level of statistical significance.

Range of Motion

Splint use in studies with no comparator group

One prospective, uncontrolled, before-and-after study by Tada et al.[14] found no significant improvement from the baseline in the range of motion test score in patients with painful OA of the DIP test after using the splint for up to six months.

Safety

One systematic review,[11] one RCT,[12] and two prospective, uncontrolled, before-and-after studies[14,15] found no adverse events were reported in either the splinting, usual care,[11,12,14,15] or local steroid injection groups.[12] In the RCT by So et al.,[13] four patients reported discomfort of wearing the splint while three patients treated with local steroid injection reported short-lasting injection site pain. The incidence rates of the side effects in the two groups in this study were not statistically significantly different. One systematic review,[2] one RCT,[13] and two prospective, uncontrolled, before-and-after studies[16,17] provided no information about adverse events.

Limitations

The primary studies of the included systematic reviews[2,11] that were relevant to the research question of this Rapid Response report were relatively few (seven in one and six in the other), and they were at high risk of bias. Further, there was significant overlap in the primary studies of the two of the systematic reviews,[2,11] with five RCTs of the six relevant studies from one systematic review[2] counted among the seven relevant RCTs in the other systematic review.[11] Thus, a significant proportion the pooled estimates presented separately by these two systematic reviews come from of the same data.

Another limitation is that the two systematic reviews[2,11] reported comparative outcomes between splints and usual care, with none of them providing a clear definition of the latter. Thus, it is unknown if the definition of usual care, as applied in the studies, referred to pharmacotherapy or will coincide with its application in the Canadian context. Therefore, it is uncertain if the reported findings with be generalizable in settings where the meaning of usual care differs from what was applied in the studies. Also, the comparator data used in meta-analysis were from usual care or no intervention without reporting separate results for either of them compared to splint. Given that lack of treatment might not result in improved

outcomes, it is unclear if splints might perform equally well in comparison with usual care alone as they did in analyses that considered data from usual care or no treatment together as comparator group.

Limitations with the RCTs[12,13] include the different duration of studies with one study lasting six weeks and the other 4 weeks. The duration-related limitation was demonstrated in the fact that though the two RCTs[12,13] investigated the comparative effectiveness of a single local injection versus splinting at night, they had inconsistent outcomes about function performance. It is unknown if the results from the studies would be in alignment if both studies went on for the same length of time. A fundamental limitation in the prospective, uncontrolled, before-and-after studies is that the different studies assessed different kinds of splints, with variations in design and materials used in construction,[14-17] as well as custom-made splints,[15] and amateur, patient-fabricated splint for personal-use.[17] That raises a generalizability question concerning whether the use of generic commercially available splints would achieve similar results as those used in the studies.

Finally, there no studies identified that compared splints to pharmacological interventions meant to relieve pain such as non-steroidal anti-inflammatory drugs, acetaminophen, topical capsaicin, and topical salicylates as well as less conventional drugs such as pregabalin and duloxetine. Also, none of the included studies[2,11-17] in this report provided outcomes on health-related quality of life, disability level, or global impression of recovery after the treatment with of any of the studied interventions.

Conclusions and Implications for Decision or Policy Making

Two systematic reviews,[2,11] two RCT,[12,13] and four prospective, uncontrolled, before-and-after studies[14-17] provided information for this report. Patients enrolled in these studies had been diagnosed with osteoarthritis of thumb base osteoarthritis (rhizarthrosis),[11] the DIP,[2,14] or TMC joints,[15] as well as CTS,[12,13,17] and tennis elbow.[16] Comparative effectiveness results were reported for splint versus usual care or no intervention[2,11] and splint versus local steroid injection.[12,13] Also, outcomes after a specified period of splinting were compared to measurements taken before commencing splint use in the same patients without comparison to another group of patients, treated or not treated.[14-17]

Evidence from the two included systematic reviews[2,11] suggested that in patients with rhizarthrosis[11] or hand OA involving the CMC, DIP, and thumb pain,[2,11] the use of splints significantly reduced pain and improved functional performance compared with usual care or no treatment in the long-term but not in the short-term. Short-term and long-term were not defined.[2,11] However, in one systematic with significant overlap of primary studies,[2] the earlier follow-up assessments that did not show a statistically significant difference in outcomes between treatment groups occurred after four to eight weeks of treatment, whereas evaluations conducted after 13 to 52 weeks of treatment showed significantly better results in favor of splint compared to usual care or no intervention. Evidence from the included systematic reviews[2,11] also suggests that compared to usual care or no intervention, splinting does not significantly improve pinch strength[11] or grip strength.[2]

Evidence from the two included RCTs[12,13] indicated that a single dose of 20 mg methylprednisolone acetate injection was statistically more significantly effective than night splitting for reducing pain intensity in patients with CTS after four to six weeks of treatment. Local steroid injection also improved figure dexterity[13] significantly, whereas the use of splint did not achieve significant improvement in this measure. However, the findings on functional performance from the two studies were inconclusive. One RCT[12] reported a

statistically significantly greater improvement in function with the steroid injection than night splinting. However, the other RCT[13] found no significant difference between the treatment groups at fourth-week follow-up assessment. It was unclear whether the different duration of the studies could explain the disagreement in the levels of statistical significance regarding differences in functional performance between local steroid injection and night splinting.

Evidence from the four prospective, uncontrolled, before-and-after studies[14-17] suggested that compared to baseline, the use of splints for four to six weeks resulted is a statistically significant reduction in pain,[14-16] improvement in functional performance,[14-17] as well as range in motion,[14] pinch strength,[15] and hand strength.[15]

Four of the included studies found no evidence of adverse events with either splinting[11,12,14,15] or local steroid injection use.[12] One RCT[12] found no statistically significant difference in the rates of the side effects between the splinting and local steroid injection groups, with four patients in the former group reporting wearing discomfort while three patients in the latter had short-lasting injection site pain. One systematic review,[2] one RCT,[13] and two prospective, uncontrolled, before-and-after studies[16,17] provided no information about adverse events.

Sources of uncertainty in the current report included the fact that the systematic reviews[2,11] were based on studies with high risk of bias as reported by the authors. Also, due to the significant overlap of primary studies between them, the evidence from the two systematic reviews[2,11] likely came mainly from the same primary studies. Furthermore, the included studies in both the systematic reviews[2,11] did not define ‘‘usual care’’. So, it was unknown if the meaning of usual care intended by the authors of the studies referred to pharmacotherapy or will coincide with the applicable definition in the Canadian context. Therefore, the generalizability of the reported findings is uncertain in settings where usual care may differ from what was intended in the studies. Also, the comparator data used in meta-analysis were from usual care or no intervention without reporting separate results for either of them compared to splint. Given that lack of treatment might not result in improved outcomes, it is unclear if splints might perform equally well in comparison with usual care alone as they did in analyses that considered data from usual care or no treatment together as comparator group.

The included primary studies[12-17] also had limitations, including the fact that they all had an open-label design study with high risk of bias due to difficulty in achieving blinding considering the intervention under investigation. Also, four out of the six primary studies were prospective, uncontrolled, before-and-after studies,[14-17] with inherently higher likelihood of systemic biases due to lack of the risk-diminishing property of randomization, and they assessed different kinds of splints. Variations were observed in design and materials used in construction,[14-17] custom-made splints,[15] and amateur fabrications of splint by patients for self-use.[17] Thus, the it was unclear if the finding of these studies could be replicated raises using generic, commercially available splints.

Furthermore, there were no studies identified that compared splints to pharmacological interventions for pain relief such as non-steroidal anti-inflammatory drugs, acetaminophen, topical capsaicin, and topical salicylates as well as less conventional medications such as pregabalin and duloxetine. Also, none of the included studies[2,11-17] in this report provided outcomes on health-related quality of life, disability level, or global impression of recovery after the treatment with of any of the studied interventions.

Future research comparing a variety of standard widely-used splints with well-defined usual care and commonly used pharmacological interventions, as well as addressing the methodological quality limitations identified in this report, is needed to more accurately determine the right place in therapy for splinting in adult patients living with chronic non-cancer pain of the upper extremities.

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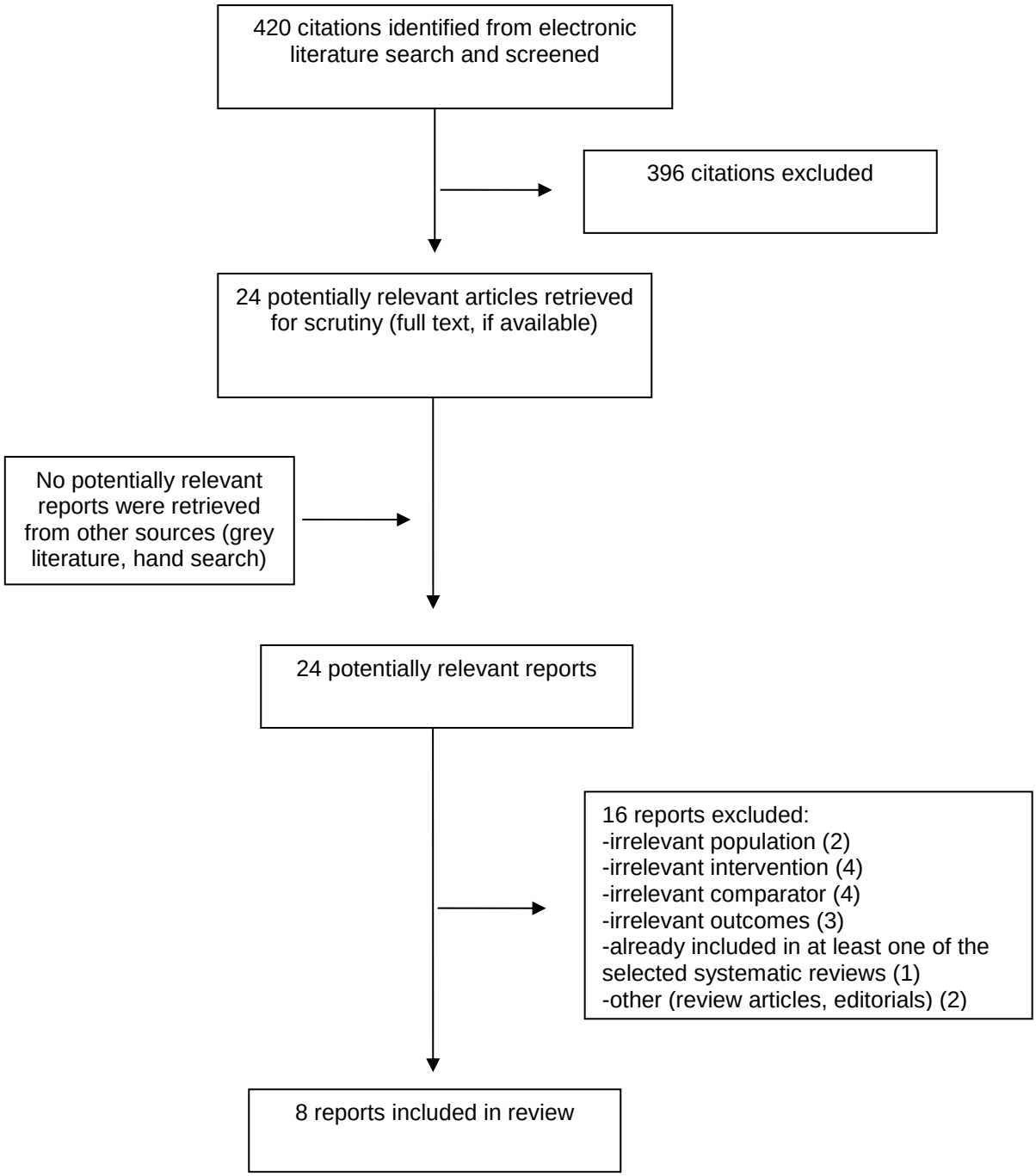
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Systematic Reviews and Meta-Analyses

Characteristics of Included Systematic Reviews

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Meireles et al., 2019[11] **Brazil**	A systematic review of 14 RCTs, including seven RCTs on orthoses that met the criteria of interest to this Rapid Response review. The remaining seven did not meet the criteria because they investigated combination interventions and/or compared different types of splints to each other and no comparator of interest.	From the seven RCTs of interest a total of 357 patient with thumb base osteoarthritis (rhizarthrosis)	Orthoses versus no interventions or usual care (not defined)	• Pain, • Function, • Pinch strength • Adverse events The duration of the patient follow-up varied between two weeks and seven years
Kroon et al., 2018[2] **The Netherlands**	A systematic review of 127 RCTs and CCTs, including 14 studies that investigated and reported outcomes after splint use. Of these 14 studies on splint six met the criteria of interest to this Rapid Response review and eight did not meet the criteria because they investigated combination interventions and/or compared different types of splints to each other and no comparator of interest.	From the six studies of interest (5 RCTs and one non-randomized CCT), a total of 315 patients with hand OA involving CMC, thumb pain, or DIP	Splint versus usual care (not defined) or no intervention	• Pain • Function • Grip Strength The follow-up was between four weeks and one year

CCT = controlled clinical trial; CMC = first carpometacarpal joint; DIP, distal interphalangeal joint; OA = osteoarthritis; RCT = randomized controlled trial.

Table 3: Characteristics of Included Primary Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Randomized Controlled Trials				
Chesterton et al., 2018[12] **The United Kingdom**	A two-arm parallel group, open-label, RCT	A total of 234 patients 18 years or older, with new episode of primary idiopathic mild or moderate CTS present for longer than 6 weeks. The mean (SD) age was 52.2 (14.9) years in the splint group 52.6 (17.0) years in the corticosteroid group, and male participants constituted 31% and 37%, respectively, in the groups.	Night-resting splint to wear for 6 weeks versus Corticosteroid (given as a single injection of 20 mg methylprednisolone acetate)	• Improvement in symptom severity and functional status • Hand-wrist symptom intensity • Adverse events Follow-up was at 6 weeks, 6 months, 12 months, and 24 months
So et al., 2018[13] **China**	A prospective RCT	A total of 50 patients, 18 years or older, with CTS. The mean (SD) age was 57.3 (9.34) years, and 86% were female	Splint to wear at night for one month (i.e., 4 weeks) versus Corticosteroid (given as a single injection of 20 mg methylprednisolone acetate premixed with lidocaine)	• Improvement in symptom severity and functional status at 4 weeks, • Change in finger dexterity • Adverse events Follow-up was at 4 weeks, 6 months, 12 months, and 24 months
Non-Randomized studies				
Tada et al., 2018[14] **Japan**	A prospective before-and-after study	A total of 30 patients with painful OA of the DIP. The mean was 68 years (range; 46 to 85 years), and 93% were female.	A tin ring splint to wear when in pain. For each patient, outcomes at follow-up assessments were compared to baseline values without a separate comparator group.	• Pain scale, • Range of motion • Function • Adverse effects Follow-up was after 1, 3, and 6 months of splint use
Maddali-Bongi et al., 2016[15]	A prospective before-and-after study	A total of 50 patients with symptomatic TMC joint OA in stages	A custom-made 'butterfly' short opponens splint of thermoplastic material	• Pain • Function • Hand strength • Pinch strength

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Italy		I–III. The mean (SD) age was 60.72 (8.7) years; 88% female	to be worn 16 hours per day for 30 days. For each patient, outcomes at follow-up assessments were compared to baseline values without a separate comparator group. All the patients participated in an educational program in which they were informed on OA and its consequences; treatment options; how to deal with OA; and education about ergonomic principles to prevent TMC overuse	• Adverse events Follow-up was at the first month and at the 12th month after splint use
Najafi et al., 2016[16] **Iran**	A prospective before-and-after study	A total of 15 patients with tennis elbow. The mean (SD) age 43 (7.69) years and 66.7% were female	A spiral hand-forearm splint. For each patient, outcomes at follow-up assessments were compared to baseline values without a separate comparator group.	• Pain (VAS) • Function • Grip strength, • Active motion Follow-up was after at four weeks of splint use.
Weng et al., 2016[17] **China**	A prospective before-and-after study	A total of 41 patients with CTS. The mean (SD) age was 50.2 (12.0) years, and 90% were female	A neutral wrist nocturnal splint. For each patient, outcomes at follow-up assessments were compared to baseline values without a separate comparator group.	• Symptom severity • Functional status The follow-up was an average (SD) of 3 (1.16) months

BCTQ = Boston Carpal Tunnel Questionnaire; CTS = carpal tunnel syndrome; DIP = distal interphalangeal joint; OA= osteoarthritis; RCT = randomized controlled trial; SD = standard deviation. TMC = trapeziometacarpal.

Appendix 3: Critical Appraisal of Included Publications

Table 4: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR 2[8]

Strengths	Limitations
Meireles et al., 2019[11]	
• The elements of PICO were described by the research questions, inclusion criteria, and other parts of the methods section. • A comprehensive literature search with no language restriction was conducted in multiple databases and supplemented by searches into annals of scientific events in the area a manual search of the studies electronically identified. Also, efforts were made to identify includable unpublished trials by searching the ClinicalTrials.gov site and WHO-ICTRP. • Two reviewers independently selected studies, conducted quality assessment, and extracted results, with arrangement to resolve conflicts through a third researcher. • The included studies were described in tabular form. • The methodological quality of the studies included was also analyzed using the Cochrane collaboration risk of bias tool[20] and the PEDro scale,[21] and the quality of the evidence was rated using GRADE. • Heterogeneity was assessed using I^2 the statistical test, and appropriate statistical models were used in pooling of results in meta-analysis, depending on the level of heterogeneity. • The discussion and interpretation of the results of the systematic review considered observed heterogeneity and RoB in individual included studies. • The authors declared no conflict of interest.	• There was no indication that the systematic review was based on a protocol written before hand and with independent verification. • The authors did not explain why they limited inclusion to RCTs. However, the study design restriction seemed justified given that RCTs rank higher than other primary studies and there were enough of them available to address the review questions. • A list of excluded studies with reasons for exclusion was not provided. • Assessment of publication bias was not conducted to evaluate any potential impact of small samples, methodological limitations in trials, or heterogeneity in interventions, populations or outcomes. • The sources of funding for the individual studies included in the systematic review were not reported
Kroon et al., 2018[2]	
• The elements of PICO were described by the research questions, inclusion criteria, and other parts of the methods section. • A comprehensive literature search with no language restriction was conducted in multiple databases and supplemented by searches in conference abstracts of the EULAR, ACR, and OARS, annual conferences as well as a manual search of the reference lists of studies identified through the electronic searches. • The included studies were described in tabular form. • The Cochrane collaboration risk of bias tool[19] was used to assess the methodological quality of the individual studies included in the systematic review. • The discussion and interpretation of the results of the systematic review considered observed heterogeneity and RoB in individual included studies. • Under a competing interest subheading, two of the four contributing authors declared receiving	• There was no indication that the systematic review was based on a protocol written before hand and with independent verification. • Study selection and data extraction was performed by one reviewer author. Thus, there was no measure to mitigate the risk of study selection bias and independent verification of extracted data was lacking. • The authors did not explain why they limited inclusion to RCTs. However, the study design restriction seemed justified given that RCTs rank higher than other primary studies and there were enough of them available to address the review questions. • A list of excluded studies with reasons for exclusion was not provided. • Although the authors reported that there was heterogeneity in many of the included studies, the method for assessing heterogeneity was not described.

Strengths	Limitations
consultancy fees and/or research funding from pharmaceutical companies. It is unknown how that had any influence on the study, or the published findings.	• All the included studies relevant to this Rapid Response report were assessed to be at high RoB, often due to lack of blinding or inadequate method of randomization. • Assessment of publication bias was not conducted to evaluate any potential impact of small samples, methodological limitations in trials, or heterogeneity in interventions, populations or outcomes. • The sources of funding for the individual studies included in the systematic review were not reported.

ACR = American College of Rheumatology; EULAR = European League Against Rheumatism; GRADE = Grading of Recommendations Assessment, Development and evaluation; OARSI = OsteoArthritis Research Society International; PEDro = Physiotherapy Evidence Database, PICO = population, intervention, comparator, and outcome; ROB = risk of bias; WHO-ICTRP = World Health Organization International Clinical Trials Registry Platform

Table 5: Strengths and Limitations of Randomized Controlled Trials using SIGN Methodology Checklist 2[9]

Strengths	Limitations
Chesterton et al., 2018[12]	
• The study objective was well-defined, and the participants were randomly assigned to one of the two treatment groups. • Calculation was performed to determine appropriate sample size that ensured the study was sufficiently powered to detect a true difference between the two intervention groups. • The enrollment of patients from multiple (25 in all) primary and community musculoskeletal clinics and services enhanced generalizability • The allocation sequence was not available to research team members, and the treatment group allocation was concealed during the analyses. • The demographic and disease condition characteristics were similar at the start of the trial across the treatment and control groups, with the interventions under investigation being the only inter-group difference at baseline. • All relevant outcomes were measured BCTQ score which is a validated and reliable disease-specific instrument. • The primary analysis was based on the intention-to-treat population. • The percentage of missing data for the various questionnaire items was generally low (≤5%) and unlikely to affect the reported results. • Missing data was handled through multiple imputation and the results based on multiply imputed data were compared with those based on complete-case analysis as a sensitivity analysis. • The study was funded by Arthritis Research UK that had no role in study design, data collection, data	• An open-label study with difficulty in ensuring blinding considering the treatment under investigation. Thus, the has inherent high risk of bias due to lack of blinding and difficulty in achieving adequate concealment. • A subgroup analysis was not performed to assess is the consistency of results from all sites (25 in all).

Strengths	Limitations
analysis, data interpretation, or writing of the manuscript.	
So et al., 2018[13]	
• The study objective was well-defined, and the participants were randomly assigned to one of the two treatment arms. • Calculation was performed to determine appropriate sample size that ensured the study was sufficiently powered to detect a true difference between the two intervention groups. • The study recruited consecutive CTS patients attending the general medical unit of a local hospital. Therefore, the study participants are likely to be a representative sample from the general patient population presenting with symptoms of CTS. • The demographic and disease condition characteristics were similar at the start of the trial across the treatment and control groups, with the interventions under investigation being the only inter-group difference at baseline. • All relevant outcomes were measured using validated and reliable instruments (BCTQ score for symptom and function, and the nine-hole peg test for figure dexterity). • All the randomized patients completed group completed the study procedures and there was no report of missing data.	An open-label study with difficulty in ensuring blinding considering the treatment under investigation. Thus, the has inherent high risk of bias due to lack of blinding and difficulty in achieving adequate concealment.

BCTQ = Boston Carpal Tunnel Questionnaire; CTS = carpal tunnel syndrome

Table 6: Strengths and Limitations of Non-Randomized Studies using RoBANS[10]

Strengths	Limitations
Tada et al., 2018[14]	
• Given that the study used the same patients in analysis for before and after intervention comparison, the risk of bias due to selection of study participant is low. • Data for the study was collected prospectively from the same consecutively recruited patients at baseline and follow-up assessments. Therefore; target group selection bias due to selective application of intervention, or due to using only participants with good outcomes in the selection process, as could potentially happen if data was collected retrospectively, was low. • Because validated instruments were used to assess outcomes at multiple timepoints during the study, the risk of confirmation bias due to inappropriate outcome assessment methods was low	• The lack of the risk-diminishing property of randomization to the intervention or a comparator indicate an inherent likelihood of systemic biases. • The investigators did not mention potential confounding factors such as natural course of disease or differences in lifestyle that may influence outcomes, and no confounder was considered during analysis or design. Therefore, there is a high potential for risk of selection bias due to inappropriate confounder confirmation and consideration. • There was no indication of any measure to ensure assessors blinding for any of the outcomes. Thus, a high potential existed for confirmation bias due to inappropriate blinding of assessors. • There was a potentially high risk of performance bias due to differences in exposure to intervention because frequency of application was not standardized, and

Strengths	Limitations
• The risk of reporting bias due to selective outcome reporting was low because most of the expected main outcomes were included.	patients were instructed to wear the splint when they felt pain. • No information was provided about compliance, dropout rate, or missing data. Thus, the risk of attrition bias due to inappropriate handling of incomplete data cannot be ruled out.
Maddali-Bongi et al., 2016[15]	
• The risk of bias due to selection of study participant is low, given that the study used the same patients in analysis for before and after intervention comparison. • Data for the study was collected prospectively from the same consecutively recruited patients at baseline and follow-up assessments. Therefore; target group selection bias due to selective application of intervention, or due to using only participants with good outcomes in the selection process, as could potentially happen if data was collected retrospectively, was low. • The risk of confirmation bias due to inappropriate outcome assessment methods was low because validated instruments were used to assess outcomes at multiple timepoints during the study, • The risk of reporting bias due to selective outcome reporting was low because most of the expected main outcomes were included. • The risk of performance bias due to inappropriate intervention or inappropriate exposure measurement was low because of standardized frequency of application, high compliance, and retention of all patient during treatment and follow-up. • Retaining all patients during the entire treatment and follow-up period without missing data also minimized the risk of attrition bias due to inappropriate handling of incomplete data.	• The lack of the risk-diminishing property of randomization to the intervention or a comparator indicate an inherent likelihood of systemic biases. • The investigators did not mention potential confounding factors such as natural course of disease or differences in lifestyle that may influence outcomes, and no confounder was considered during analysis or design. Therefore, there is a high potential for risk of selection bias due to inappropriate confounder confirmation and consideration. • There was no indication of any measure to ensure assessors blinding for any of the outcomes. Thus, a high potential existed for confirmation bias due to inappropriate blinding of assessors.
Najafi et al., 2016[16]	
• The study used the same patients in analysis for before and after intervention comparison. Thus, the risk of bias due to selection of study participant is low. • All patients were referred by an orthopedic specialist, and they all provided data collected prospectively at baseline and follow-up assessments. Therefore; target group selection bias due to selective application of intervention, or due to using only participants with good outcomes in the selection process, as could potentially happen if data was collected retrospectively, was low. • All assessments were conducted by the same orthotist who was trained to administer the tests using validated instruments. Therefore, the risk of confirmation bias due to inappropriate outcome assessment methods was low.	• The lack of the risk-diminishing property of randomization to the intervention or a comparator indicate an inherent likelihood of systemic biases. • The investigators did not mention potential confounding factors such as natural course of disease or differences in lifestyle that may influence outcomes, and no confounder was considered during analysis or design. Therefore, there is a high potential for risk of selection bias due to inappropriate confounder confirmation and consideration. • The assessor was not blinded to the measurement of any of the outcomes. Thus, a high potential existed for confirmation bias due to inappropriate blinding of assessors.

Strengths	Limitations
• The risk of performance bias due to inappropriate intervention or inappropriate exposure measurement was low because of standardized frequency of application, high compliance, and retention of all patient during treatment and follow-up. • All patients continued their use of the splint to the end of the study and there was not report of missing data. Thus, the risk of attrition bias due to inappropriate handling of incomplete data was low. • The risk of reporting bias due to selective outcome reporting was low because most of the expected main outcomes were included.	
Weng et al., 2016[17]	
• The risk of bias due to selection of study participant is low, given that the study used the same patients in analysis for before and after intervention comparison. • Thus, the risk of reporting bias due to selective outcome reporting was low because most of the expected main outcomes were included.	• The lack of the risk-diminishing property of randomization to the intervention or a comparator indicate an inherent likelihood of systemic biases. • Although data for the study was collected prospectively from the same consecutively recruited patients at baseline and follow-up assessments, the risk of selection bias due to inappropriate intervention could not be ruled out because each patient were instructed to make and use their own splint, which likely resulted in variations with potential to influence outcomes. • The investigators did not mention potential confounding factors such as natural course of disease or differences in lifestyle that may influence outcomes, and no confounder was considered during analysis or design. Therefore, there is a high potential for risk of selection bias due to inappropriate confounder confirmation and consideration. • Although a symptom severity scale and a functional status scale were used to evaluate the patients at each hospital visit, it was unknown if these were validated tools. Thus, the risk of confirmation bias due to inappropriate outcome assessment methods cannot be ruled out. • There was no indication of any measure to ensure assessors blinding for any of the outcomes. Thus, a high potential existed for confirmation bias due to inappropriate blinding of assessors. • There was a potentially high risk of performance bias due to differences in exposure to intervention because frequency of application was not standardized, and patients were instructed to wear the splint when they felt pain. • No information was provided about compliance, dropout rate, or missing data. Thus, the risk of attrition bias due to inappropriate handling of incomplete data cannot be ruled out.

Appendix 4: Main Study Findings and Authors' Conclusions

Table 7: Summary of Findings Included Systematic Reviews

Main Study Findings	Authors' Conclusion
Meireles et al., 2019[11]	
Pain Short-term • Meta-analysis of data from two studies (n = 141) found no significant difference in pain between splint and no intervention or usual care. ES (range) = -0.29 (-1.00 to 0.42); P = 0.42, (quality of evidence was graded low) Long-term • Meta-analysis of data from three studies (n = 203) found a statistically significant difference in long-term pain in favor of splint and over no intervention or usual care. ES (range) = -0.52 (-0.94 to -0.11); P = 0.01, (quality of evidence was graded low) **Function** Short-term • Meta-analysis of data from two studies (n = 141) found no significant difference in function between splint and no intervention or usual care. ES (range) = 0.11 (-0.22 to 0.44]); P = 0.53, (quality of evidence was graded moderate) Long-term • Meta-analysis of data from three studies (n = 201) found a statistically significant difference in long-term function in favor of splint and over no intervention or usual care. ES (range) = -0.44 (-0.72 to -0.15); P = 0.002, (quality of evidence was graded moderate) **Pinch Strength** Short-term • Meta-analysis of data from two studies (n = 142) found no significant difference in pinch strength between splint and no intervention or usual care. ES (range) = -0.02 (-0.35 to 0.31); P = 0.91, (quality of evidence was graded moderate) Long-term • Meta-analysis of data from two studies (n = 136) found no significant difference in long-term pinch strength between splint and control. ES (range) = -0.18 -0.52 to 0.16); P = 0.30, (quality of evidence was graded moderate) **Adverse events** • No side-effect was described regarding the use of orthosis for rhizarthrosis.	From meta-analysis of data from relevant studies, the authors "concluded that orthosis for rhizarthrosis presents low-quality evidence for pain reduction in the long term and moderate evidence for an increase in function in the long term." (p. 788)
Kroon et al., 2018[2]	
For findings from the included RCTs and non-randomized studies, the risk of bias in the studies was rated as high, and the quality of evidence ranged from low to very low.	In the long-term (i.e., 13 to 52 weeks) splinting of the thumb base was shown to result in significant symptom relief in the area of pain reduction and improvement function.

Main Study Findings	Authors' Conclusion
Pain • Meta-analysis of data from four studies (n = 221) found that after 4 to 8 weeks of treatment, the reduction in pain for patient who used thumb splint was not statistically significantly higher than usual care or no intervention (MD = −2.9; 95% CI −12.2 to 6.5) on 100 mm VAS. However, meta-analysis of two of the studies (n = 137) found a significant between-group difference in pain in favor of thump splint after 13 to 52 weeks of treatment (MD −17.4; 95% CI −25.6 to −9.2) on 100 mm VAS. • One RCT (n = 26) found no statistically significant difference in pain between patients who used DIP splint and those who received no intervention after 12 weeks of treatment (median difference on 10 cm VAS was 0.5 (range −7 to 3.5, P = 0.53). **Function** • Meta-analysis of data from three studies (n = 144) found that after 4 weeks of treatment, the improvement in function for patient who used with thumb splint was not statistically significantly higher than usual care or no intervention compared to usual care or no intervention (SMD = −2.4; 95% CI −0.11 to 0.60) on 100 mm VAS. However, one of the studies (n = 112) found a significant between-group difference in function in favor of thump splint after 52 weeks of treatment (MD −6.3; 95% CI −10.9 to −1.7) on Cochin hand function scale (range 0–90). • One RCT (n = 26) reported that after 12 weeks of treatment there was no between-group difference in function for patients who used DIP splint and those who received no intervention. Specific data were not presented for this outcome. **Grip Strength** • Meta-analysis of data from two studies (n = 95) found that improvement in grip strength was not statistically significantly different for patients who used thumb splits compared to usual care or no intervention, after 6 to 8 weeks of treatment (SMD = 0.39 (95% CI−0.35 to 1.1) One of the studies (n = 40) found that the between-group difference in grip strength was not statistically significant after 13 weeks of treatment MD = 0.8 (−3.1 to 4.7) kg.	

CCT = clinical controlled trial; CI = confidence interval, DIP = distal interphalangeal joint; ES = effect size; MD = mean difference; RCT = randomized controlled trial; SMD = standardized mean difference; VAS = visual analogue scale.

Table 8: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
Chesterton et al., 2018[12]	
Pain • At six weeks follow-up assessment, patients treated with a single corticosteroid injection after randomization showed significantly better improvement hand-wrist pain intensity than those who wore night splints for six weeks (aMD = –0·97, 95% CI –1·64 to –0·30; P = 0·0049). • Compared to baseline, the mean (SD) score of hand-wrist pain intensity had decreased at the six weeks follow-up assessment as follows: ○ Corticosteroid injection group – from 6·33 (2·05) to 3·42 (2·77) ○ Night splint group – from 6·12 (2·21) to 4·28 (2·73) **Symptom and Function (BTCQ scores)** • At six weeks follow-up assessment, the improvement in overall BCTQ score in the corticosteroid injection group was significantly better than in the night splint group as indicated by the aMD –0·32; 95% CI –0·48 to –0·16; P = 0·0001). • The aMD for BCTQ subscales were consistent with the overall results in showing better outcomes with corticosteroid injection than night splint at six weeks: ○ Symptom severity: –0·35 (95% CI –0·53 to –0·17; P = 0·0001) ○ Functional limitations: –0·26 (–0·43 to –0·09; P = 0·0031) • At the individual group level, the six weeks follow-up assessment showed that the overall mean BCTQ score had decreased from 2·69 (SD 0·70) at baseline to mean 2·02 (0·81) in the corticosteroid injection group, and from 2·65 (0·62) to 2·29 (0·75) in the night splint group, signifying improvement in symptom severity and functional limitation in both groups. **Adverse events** • No adverse events were reported for either the corticosteroid or splint groups.	"single corticosteroid injection shows superior clinical effectiveness at 6 weeks compared with night-resting splints, making it the treatment of choice for rapid symptom response in mild or moderate carpal tunnel syndrome presenting in primary care."[12] (p. 1423)
So et al., 2018[13]	
Symptom and Function (BTCQ scores) • There was no statistically significant difference between the night splinting and corticosteroid groups in the overall BTCQ scores and its FSS and SSS subscales after four weeks treatment ○ The mean overall score change (SD) in the steroid group was -0.443 (0.426) compared with -0.20 (0.351) in the splinting group (P = 0.22) ○ The mean SSS change (SD) in the steroid group was -0.670 (-0.614) compared with -0.38 (0.475) in the splinting group (P = 0.07).	"Although local steroid injection and nocturnal wrist splinting were equally effective in the treatment of patients with CTS, only the former improved objective hand function. Local steroid injection also resulted in better patient satisfaction and less painkiller use without causing more side effects."[13] (p.1)

Main Study Findings	Authors' Conclusion
○ The mean FSS change (SD) in the steroid group was -0.190 (0.364) compared with -0.21 (0.342) in the splinting group (P = 0.873). • However, at the fourth-week follow-up, statistically significant improvements had occurred (compared with baseline) in both groups with respect to the overall BCTQ score and the SSS and FSS subscales with P values ranging from 0.05 to <0.0001 **Finger dexterity** • For figure dexterity, patients in the steroid group had significant improvement 4 weeks after the local injection as indicated by the median change in the nine-hole peg test score of -2.56 (range: -9.47 to 7.73; P = 0.038). However, the change in the nine-hole peg test in the splinting group did not reach the level of statistical significance after four weeks of treatment (-1.19 [range: -7.46 to 7.91; P = 0.065). The intergroup difference was not statistically significant (P = 0.16). **Adverse events** • Four patients in the splinting group reported discomfort when wearing the splint and three patients treated with local steroid injection short-lasting pain after the injection. The incidence rates of the side effects in the two groups were not statistically significantly different.	
Tada et al., 2018[14]	
Pain • The mean (SEM) pain score on a NPRS decreased significantly from 58.4 (4.1) at baseline to 33.1 (4.5) after one month of splint use (P < 0.001), • Twenty-five patients (83.3%) reported pain relief with splint use, with lessening symptoms commonly reported by the 10th day after treatment. Five patients (16.7%) reported no change. **Function** • The functional assessment, as measured by Hand 20, showed a significant improvement from the mean score of 35.0 (4.3) at baseline to 20.2 (3.2) after 6 months (P < 0.001). **Range of motion** • The range of motion test did not show a significant improvement from a mean score of 35.0 (4.1) at baseline at any of the follow-up assessments (i.e., 37.3 (4.2) after one month, 39.1 (4.3) after three months, and 39.5 (4.3) after six months).	"A tin ring splint quickly reduced pain, and satisfaction related to usability and appearance was high. This splint could be one choice for conservative treatment of osteoarthritis of the distal interphalangeal joint." (p. 684)
Maddali-Bongi et al., 2016[15]	
Pain • After one month of using splint, pain at the treated hands reduced from a mean score of 5.99 (2.47) to 2.61 (2.10) on a 0 to 10 NPS (P < 0.0001). The improvement remained significant at the 12-month	"In conclusion, the application in a clinical daily setting of a custom-made thermoplastic short opponens splint during waking hours implemented with an educational program, followed by its occasional use on pain exacerbation, resulted in an useful conservative treatment in symptomatic TMC OA in

Main Study Findings	Authors' Conclusion
follow-up assessment relative to the baseline with mean (SD score of 3.22 (2.47); (P < 0.0001). The difference in pain relief gained by the one- month and 12-month assessments was not statistically significant **Function** • Hand function and ability, as evaluated on the Dreiser scale, improved significantly from baseline mean (SD) score of 6.8 (6.06) to 4.42 (4.82); P = 0.001 at one-month follow-up assessment. **Hand strength** • Assessment dynamometer showed significant improvement in overall mean (SD) hand muscle strength from a baseline scores of 37.46 (9.05) to 49.64 (13.87) after one month of splint use (P < 0.0001) **Pinch strength** • Evaluation by a pinch gauge in kilograms showed significant improvement in overall mean (SD) pinch strength from a baseline scores of 4.52 (1.22) to 5.17 (0.90) at the one -month follow-up assessment (P < 0.0001) **Adverse events** • No patient was lost during treatment and follow-up and no side effects were reported	manual and non-manual workers and underlines the need for a tight collaboration between rheumatologists and physiotherapist skilled in rheumatic diseases in the daily clinical practice."[15] (p. 6)
Najafi et al., 2016[16]	
The following are results after four weeks of using the spiral splint **Pain** • Pain was significantly relieved as indicated by a reduction in the mean (SD) score from 8 (0.756) at baseline to 2.6 (1.59); P < 0.001. The assessment was done on a 0 – 10 VAS, where 0 = no pain, 10 = the most severe pain **Function** • A reduction in the mean (SD) DASH score from 20.74 (2.71) at baseline to 8.99 (3.57) at the four-week assessment (P < 0.001) indicated a significant improvement in function **Grip strength** • The mean (SD) grip force increased from 7.87 (2.27) at baseline to 8.99 (3.57) after 4 weeks of splint application; P < 0.001	"The new splint design had a positive effect on the treatment of tennis elbow symptoms which included pain, grip strength, and function. Restriction of rotational movement (e.g. reduction of the supination and pronation of forearm) may have played the main role in this." (p. 363)
Weng et al., 2016[17]	
Of the 41 patients CTS enrolled, outcome data were available for 20 (48.8%) who completed the follow-up assessments at an average of 3 (1.16) months. **Symptom severity** • The SSS score declined significantly from a mean (SEM) of 1.77 (0.38) at baseline to 1.55 (0.38) at follow-up assessment indicated significant improvement (P < 0.001) in symptom severity	"In conclusion, neutral wrist nocturnal splinting is effective in at least the short term in patients with CTS. There is a weak correlation between the clinical scores and NCS, which suggests that both approaches should be used to assess the therapeutic effect of treatment on CTS." (p. 2277)

Main Study Findings	Authors' Conclusion
Functional status • The FSS score decreased significantly (P < 0.001) from a mean (SEM) of 1.53 (0.31) at baseline to 1.40 (0.27) at the follow-up assessment indicating significant improvement in functional status.	

aMD = adjusted mean difference; BCTQ = Boston Carpal Tunnel Questionnaire; CI = confidence interval; CTS = carpal tunnel syndrome; FSS = functional status scale; NCS = nerve conduction studies; SD = standard deviation; SE = standard error; SME = standard error of mean; SSS = symptom severity scale

Appendix 5: Overlap between Included Systematic Reviews

Table 9: Primary Study Overlap between Included Systematic Reviews

Primary Study Citation	Systematic Review Citation	
	Meireles et al., 2019[11]	Kroon et al., 2018[2]
Adams et al., (2014)[22]	X	X
Arazpour et al., (2017)[23]	X	X
Bani et al., (2013)[24]	X	
Carreira et al., (2010)[25]	X	X
Hermann et al., (2014)[26]	X	X
Kjeken et al., (2011)[27]	X	
Rannou et al., (2009)[28]	X	X
Watt et al., (2014)[29]		X