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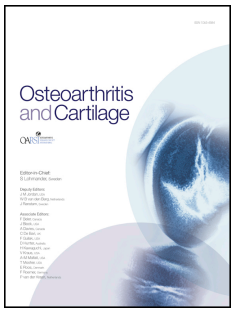

Effectiveness of splinting for pain and function in people with thumb carpometacarpal osteoarthritis: a systematic review with meta-analysis

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Effectiveness of splinting for pain and function in people with thumb carpometacarpal osteoarthritis: a systematic review with meta-analysis

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Objective: To examine the effectiveness of splinting for reducing pain and improving function and health-related quality of life (HR-QoL) in people with thumb carpometacarpal osteoarthritis (CMC OA).

Design: The Cochrane Library, MEDLINE, Embase, CINAHL, ISI Web of Science, Scopus and Google Scholar, 3 trial registries and 4 conference proceedings were systematically searched for randomised and non-randomised controlled trials up to March 17th, 2018. Two reviewers independently applied the inclusion criteria to select potential studies and assess risk of methodologic bias using the Cochrane Collaboration's Risk of Bias Tool. Studies were pooled using the inverse variance method to calculate standardised mean difference (SMD). Sensitivity analyses were conducted and the quality of evidence for each outcome was judged following the GRADE approach.

Results: Twelve studies were retrieved (n=1353), 4 comparing a splint to control and 8 to another splint. In the medium-term (3-12 months), low quality evidence showed that splints cause a moderate to large reduction in pain (SMD 0.7 [95% CI 1.04, 0.35], $P < 0.0001$) and small

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to moderate improvement in function (SMD 0.42 [95% CI 0.77, 0.08], *P* = 0.02). No significant effect was found at short-term or for different types of splints. No studies reported HR-QoL.

Conclusions: Splinting demonstrated a moderate to large effect for pain and small to moderate effect for function in the medium-term but not in the short term. Quality of the evidence is low. Major challenges are the lack of diagnostic criteria and of a gold-standard outcome measure for thumb CMC OA.

Key Words: Thumb; Trapeziometacarpal; Osteoarthritis; Splints; Systematic Review;, Meta-Analysis

Running title

Splinting for thumb CMC OA

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Introduction

Thumb carpometacarpal osteoarthritis (CMC OA) is a highly prevalent chronic condition that causes pain, limits hand function, and interferes with health-related quality of life (HR-QoL)[1-3]. The age-adjusted prevalence of radiographic thumb CMC OA is estimated at 15% for women and 7% for men age 30 years and over[4], with prevalence increasing with older age. An estimated 22% of the general population aged 50 years and over have symptomatic thumb CMC OA[5]. The natural history of thumb CMC OA in many cases involves progression to less symptomatic or stable end stage disease[6, 7].

Surgical intervention can provide relief but is usually reserved as the last option and joint replacement has not proven as successful as for hip or knee OA[8, 9]. Pharmacological treatments carry risk such as adverse gastrointestinal, cardiovascular and renal events resulting from nonsteroidal anti-inflammatory drug, especially in the older population[10]. Therefore, interventions that reduce the need for drug therapy or surgical intervention are highly desirable. Splinting is a biomechanical intervention that aims to provide external support to the CMC joint, to reduce pain, prevent contracture, and maintain hand function[11].

Clinicians commonly prescribe splints[12, 13] and clinical studies have shown positive results with significant reductions in pain and reduced demand for surgery[14-16]. International treatment guidelines conditionally recommend the use of splints for thumb CMC OA; however, the strength and quality of the evidence is variable[17, 18]. Furthermore, splints are made from a variety of materials and are of varied designs, with evidence lacking as to which is the most effective [8].

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Previous systematic reviews have examined the effectiveness of splinting for thumb CMC OA, with mixed results. In seven prior systematic reviews, four made no recommendations due to methodological limitations of the included studies[19-22], two concluded there was high to moderate level of evidence for use of splints[23, 24], and one concluded 'fair' level of evidence for the use of splints[25]. In two prior meta-analyses, one found splints reduced pain at short- and long-term follow up (although long-term was > 3 months)[26], while a recent meta-analysis found no effect for pain or function at ≤ 45 days or ≥3 months[27].

The inconsistent findings of these previous reviews reflect the small number and heterogeneity of the original studies, the small sample size of included studies and in the older reviews flawed methods for determining study quality and judging the overall strength of evidence. Recently, several primary studies have been published which may strengthen the evidence on which to base clinical recommendations. An attempt at resolving previous inconsistencies using current best practice methodology, is needed.

Considering the above, the primary aim of this current review is to perform a systematic review to investigate the effectiveness of splinting in people with thumb CMC OA for reducing pain and increasing function and HR-QoL. A secondary aim is to examine the comparative effectiveness of different splint types.

METHODS

The recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Statement guidelines were followed[28]; the full protocol is available in the public domain (PROSPERO registration: CRD42016032612).

Search strategy

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The electronic databases Cochrane Central Register of Controlled Trials, MEDLINE (OVID), Embase (OVID), CINAHL, ISI Web of Science, Scopus and Google Scholar were searched from inception to March 17th, 2018. To identify ongoing or recently completed trials we screened trial registries (WHO International Clinical Trials Registry Platform, ClinicalTrials.gov, and Australia New Zealand Clinical Trials Registry) and conference proceedings (the Osteoarthritis Research Society International, the British Society for Rheumatology, European League Against Rheumatism, American College of Rheumatology).

A comprehensive search strategy was developed using the PICOS (Population, Intervention, Comparison, Outcome and Study design) framework. Medical subject headings and text terms describing thumb CMC OA were combined with terms describing the interventions (see Supplementary Appendix 1). The search strategy was adapted for each information source. No study type or language restriction was applied. Each database was searched independently by two researchers (MB and BS). Reference lists of previous systematic reviews and included studies were searched manually for any additional studies.

We included studies investigating the effect of splinting for pain, function or HR-QoL among participants age ≥18 years with a diagnosis of thumb CMC OA (as defined by the authors of the included trials). Control/comparator interventions included any other surgical or non-surgical intervention (including an alternate splint), no intervention, or sham intervention. Randomised controlled trials (RCT) and quasi-experimental studies were eligible for inclusion. No restriction was made on study setting.

The primary outcome variable of interest was pain. The primary safety outcome was withdrawal due to adverse events. Secondary outcome variables of interest were measures of physical function or disability (self-reported or performance measure) and measures of

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HR-QoL. Where multiple measures were reported for the same outcome, decisions about which outcome measure data to extract where made according to a pre-specified hierarchy (see PROSPERO protocol 2016:CRD42016032612). Follow up time points were categorised as short-term (<3 months), medium-term (3-12 months), and long-term (>12 months), from time of group allocation.

Feasibility studies and studies where a splint was applied after surgery for thumb OA were excluded.

Study selection

All citations from database searching were exported to bibliographic software (EndNote X7, Thomson Reuters) and duplicates removed. Two researchers (MB and BS) independently screened titles and abstracts for possible inclusion. Potentially eligible studies were obtained in full text and independently assessed for inclusion. Any disagreement was resolved in the first instance by discussion, and where required in consultation with a third reviewer (CC). Consultation occurred in five cases and was resolved.

Data extraction

Data were extracted using a form tailored and piloted for purpose. Data on the type of study, participant characteristics, intervention characteristics, outcome measures, follow up and outcomes were extracted by one researcher (MB) and cross-checked by a second researcher (BS). Authors were contacted to obtain or clarify missing or unclear data. Data only available in graph form were extracted using a freely-available web-based tool (http://arohatgi.info/WebPlotDigitizer/).

Critical appraisal of risk of methodologic bias

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Critical appraisal of risk of methodologic bias of each study was undertaken independently by two researchers (MB and BS) using the Cochrane Collaboration's 7-item Risk of Bias Tool to rate each item for each outcome as Yes/No/Unclear[29]. Risk of detection bias was scored for each outcome; subjective patient-reported outcomes (PROs) completed by unblinded participants were deemed at high risk of detection bias. Judgements were compared for discrepancy and any disagreement resolved by discussion with a third reviewer (CC).

Data synthesis and analysis

Data analysis and interpretation were performed by the first reviewer (MB) and cross-checked by a second reviewer (BS). Presentation of descriptive and inferential statistical information was made for each study. Study design, population characteristics, intervention parameters, outcome measures, and main findings were summarised. Narrative synthesis of all included studies was undertaken in the first instance.

Studies were to be included for quantitative synthesis where these met the minimum threshold for risk of methodologic bias. However, due to the small number of studies identified, the published protocol was amended to include all studies in meta-analysis in the first instance, followed by sensitivity analysis based on risk of bias threshold. Owing to the inherent difficulty of blinding participants and providers in rehabilitation research and the frequent use of subjective PROs, risk of bias threshold was amended such that only those studies judged to be at high or unclear risk of selection bias (pertaining to randomisation and/or allocation concealment) were excluded. Risk of selection bias has been shown to have the biggest impact on direction and magnitude of bias in studies of intervention effect[29].

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Clinical heterogeneity was assessed in the narrative synthesis, such that major differences between trials in the terms of study populations, interventions, and outcome measures were identified. Statistical heterogeneity was evaluated using the chi^2 test (with statistical significance set at $P < 0.10$), and the I^2 statistic computed and interpreted such that ≥50% represented substantial heterogeneity[30].

Quantitative synthesis was undertaken in Review Manager (RevMan) software (version 5.3, Cochrane Collaboration) using the inverse variance method. Standardised mean differences (SMD) and 95% confidence intervals (CI) were calculated to synthesise continuous outcomes. The random-effects model was used as heterogeneity was anticipated to be present. To aid interpretation 95% prediction intervals (PI) were calculated for analyses including three or more studies that met the minimum threshold for risk of methodologic bias[31]. Stata Version 15.1 statistical package (StataCorp LLC, College Station, TX) was used with the Hedges' g option selected.

Effect sizes were interpreted as 0.2 (small), 0.5 (medium) or 0.8 (large) [32]. The quality of the body of evidence was judged to be 'High', 'Moderate', 'Low' or 'Very Low' for each outcome following the Grades of Recommendation Assessment, Development and Evaluation (GRADE) approach[33]. Quantitative synthesis was undertaken by one reviewer (MB) and checked by second reviewer (BS) with any uncertainties regarding data preparation and computation resolved by a consultant health-sciences biostatistician.

RESULTS

Study selection

After removal of duplicates 1353 records were identified, with 12 studies (four comparing splint versus no splint, eight comparing different types of splints) meeting eligibility criteria

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for inclusion in quantitative synthesis (Figure 1). Of the included studies, nine authors provided additional information about study characteristics or result data[14, 15, 34-40].

Study characteristics

Characteristics of the included studies are reported in Table 1. Study settings were outpatient therapy clinics. Participant ethnicity was reported in one study, in which 32.5% were reported as "non-white" [sic][15]. In three studies a majority of participants were in employment[14, 38, 41] and in two studies a smaller proportion were in work[36, 42]. The remaining studies did not report work status.

Interventions comprised a range of splint designs and materials (Table 1). Rationales proposed for splint interventions included: to stabilise the CMC joint[34, 37-43]; to prevent adjacent metacarpophalangeal (MCP) joint hyperextension[14, 15, 34, 39]; to leave adjacent joints free for unhindered function[34, 39, 40, 42, 43]; to maintain length of the first web space[14, 15]; to reduce CMC joint synovitis/inflammation[36, 39, 41]; to reduce local muscle spasm[41]; for patient preference[36]. One study reported telephone follow-up at 1-week[41]. Remaining studies reported follow-up, *"only if need adjusting"* or not specified.

Pain was assessed using a variety of numerical scales (Table 1). Function used various patient-rated outcomes (PROs) except for two studies from which a performance measure (pinch grip strength) was extracted[37, 38] (Table 1). Pain and function outcomes were not reported beyond one year. Quality of life was not assessed in any of the studies, either at baseline or follow up.

Design of the included studies are listed in Table 1. Of the four cross-over design trials, two used paired-t tests to assess the effect of splint wearing[41, 42] and two used repeated-measures analysis of variance (ANOVA)[37, 38]. Funding was not received in three studies[39, 40,

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[43]; four studies received institutional or national health organisation grants[14, 15, 36, 38]; two studies received complimentary splint materials from the manufacturer[34, 41] (one stated specifically no influence on the study design, conduct or outcome[41]); and in three studies funding sources were not stated[37, 42] or unclear[35].

Risk of bias and quality assessment

One of four studies comparing splint with no splint[43] and five of eight studies comparing different types of splints[34, 37-40] were judged to be at high or unclear risk of selection bias. All outcomes reported in this review were judged to be at high risk of detection bias primarily due to PROs being completed by unblinded participants. Risk of selective outcome reporting was judged unclear or high for seven studies as study protocols were neither registered a priori nor published[34, 37, 38, 40, 43], stated outcomes or time points were not reported[14, 36], or splint materials were provided by industry with unclear risk of influence[34].

Risk of 'other' bias was judged unclear or high in 10 studies relating to four main areas: short or no washout period in cross-over design trials[37, 38, 41, 42]; potential for contamination between groups where participants in the control group were fitted with the intervention splint during assessment[15]; inconsistency in unit of allocation vs analysis (individual vs hand)[36]; and poor quality of data reporting and/or outcome ambiguity[34, 37, 39, 40]. The authors' judgements in the current review are summarised for all included studies in the risk of bias graph (Figure 2).

Further assessment of study quality identified that six studies did not state an intention-to-treat analysis or did not state or did not meet sample size calculations[34, 37, 38, 40, 41, 43]. In seven of the twelve included studies it was unclear if co-interventions were avoided or similar[34-38, 41, 43]. Acceptable adherence to the intervention(s) was reported in four studies[14,

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[38, 39, 41, 43] and variable adherence reported in two studies[36, 42]. Adherence was not reported in the remaining studies. Participant drop-out was ≤15% in all but two studies[34, 35].

Narrative synthesis

Results of the individual studies are summarised in Table 2. In all studies splints were associated with a reduction in pain scores over the course of the study (Table 2). In some studies, function worsened in the short-term[14, 37, 38, 43] or remained unchanged[41] (Table 2).

Heterogeneity was present between studies in control over potential sources of bias and in some study characteristics. Major differences were the wide range of outcome measures used and the variations in intervention implementation. Other differences included time to follow up and symptom severity (Table 1).

No major adverse events were reported; one minor adverse event of skin irritation resulted in discontinuation of splint treatment[41].

Quantitative synthesis

Effectiveness of splinting on pain and function

Synthesis of the four studies that reported on the effectiveness of splints for pain and function is reported in Figure 3. No significant effect was found for either outcome in the short-term (0-3 months) (Figure 3). This result did not alter with sensitivity analyses (Figure 4). GRADE: Very low (serious risk of bias, very serious imprecision).

Based on the overall pooled effect estimate from two studies totalling 137 participants, splinting was found to result in a statistically significant reduction in pain at medium-term (3-12 months) compared to no splinting (SMD 0.7 [95% CI 1.04, 0.35], $P < 0.0001$),

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representing a moderate to large effect size (Figure 3). GRADE: Low (serious risk of bias, serious imprecision).

The overall pooled effect estimate, from two studies totalling 135 participants, also suggested that splinting resulted in a statistically significant improvement in function at medium-term (3-12 months), (SMD 0.42 [95% CI 0.77, 0.08], *P* = 0.02), representing a small to moderate effect size (Figure 3). GRADE: Low (serious risk of bias, serious imprecision).

Outcomes at medium-term did not alter with sensitivity analysis (Figure 4).

Effectiveness of different splint types on pain and function

The effect estimate based on one study totalling 84 participants suggested that splints not including the MCP joint compared to splints including the MCP joint resulted in statistically significant improvement in function at medium-term (3-12 months) (SMD 1.68 [1.18, 2.19]) (Figure 5). GRADE: very low (very serious risk of bias, very serious imprecision).

All other comparisons showed no significant effect (Figure 5). GRADE: Very low (very serious risk of bias, very serious imprecision). Sensitivity analyses showed no significant effect for comparisons of splint type (GRADE: very low) (Figure 6).

Predication intervals were calculated for comparison of effectiveness of splints in the short-term for pain [PI -4.30, 3.94] and function [PI -1.72, 1.92] (Figure 4). No other comparisons met criteria for calculating prediction interval.

Discussion

In this systematic review we examined the effectiveness of splinting for pain and function in thumb CMC OA and compared different splint materials and design. Meta-analysis of studies without selection bias found that splints cause a moderate to large reduction in pain

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and a small to moderate improvement in function in the medium- (3-12 months) but not short-term (<3 months) (low quality of evidence). Meta-analysis of studies without selection bias found no difference between rigid and soft splints or between splints including or not including the MCP joint (very low quality of evidence). The effect of splints on quality of life in people with thumb CMC OA is unknown. We found no evidence that splints cause significant harm. Our findings of a moderate to large effect for pain and a small to moderate effect for function in the medium-term (3-12 months) are comparable to those of a previous systematic review with meta-analysis by Kjeken et al.[26]. The current review differs from a further previous systematic review (with meta-analysis) which concluded no significant effect of splinting on pain levels at ≥3 months[27]. These conflicting conclusions may be partly explained by the previous review's inclusion of one study with multiple co-interventions which did not meet inclusion criteria for the current review.

In contrast the current study found no effect of splinting for pain in the short-term (<3 months), concurring with findings in the same review.[27], whereas a significant (small to moderate effect) was found by Kjeken et al.[26]. This difference from Kjeken et al. may be explained by our inclusion of a more recent study investigating a soft rather than rigid splint which reported relatively poor adherence to splint wearing[36]. Our finding of no significant difference between splint material or design concurs with that of a previous systematic review[44].

This systematic review provides a robust updated appraisal of the evidence for splinting in people with thumb CMC OA and examines characteristics of the study designs and splint interventions. Splinting is a promising non-invasive intervention for thumb CMC OA which is

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an extremely prevalent condition. From current evidence conditional recommendations can be made for the benefits of splinting and the lack of harm in clinical practice.

Study limitations

The small number of original studies and the small sample size of each included study represents a significant limitation of the current and previous reviews. Meta-analysis with such small sample sizes may be at risk of 'small sample bias'[45]. That is, issues of lower methodological quality along with reporting biases combine to result in the reporting of larger effect sizes than those in larger trials[45]. These issues are evident in the current review by the high rate of selective outcome reporting, the ubiquitous risk of detection and performance bias, and by the smaller effect sizes seen on sensitivity analysis. However, publication bias while likely to be present to some extent, is not strongly suspected as most of the included studies are not industry sponsored or likely to be industry sponsored[46]. The use of funnel plots was not warranted given the small number of included studies[47].

These methodological issues are also apparent in the statistical heterogeneity in the current review that is present for the comparison of splint versus no splint for pain, (Figure 3, Figure 4), and substantial for comparisons between splint types (Figure 5) at the short-term. Although heterogeneity relating to risk of bias will tend to have overestimated the effect sizes, the impact of heterogeneity in other study parameters (outcome measures, intervention implementation and population characteristics), is underestimation.

Prediction intervals calculated for the comparison of splint vs no splint outcomes at short-term indicate that it is probable that 95% of exchangeable studies in the future can be expected to produce effects within these intervals ([PI -4.30, 3.94] and [PI -1.72, 1.92], for pain and function, respectively), both of which span the null (Figure 4). Clearly, further new studies are likely to add significantly to the current evidence base, if performed to a high

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standard using Cochrane supported methodology and following the PREPARE Trial guidelines[48]. Symptom type and severity may be potential subgroupings for future primary studies and/or meta-analysis.

The study design best suited to provide further evidence for the effectiveness of splints is one which includes a control group and is randomised but not with a cross-over design. Only three of the studies in this review included a control group[14, 15, 36]. The cross-over randomised-trial design was used by four of the studies in this review, with data from two included in sensitivity analysis in the comparisons of splint material[42] and splint design[41, 42]. The use of cross-over design is problematic in studies of thumb CMC OA since it is a chronic condition; if splint interventions are to be worthwhile they need to be effective over a prolonged period of follow up. The cross-over designs included in this review required the treatment effect to be lost after a short washout period (1-2 weeks). Further, statistical checking of carry over effect is considered imperfect[49] and possible bias due to carryover effect remains a concern. The inclusion of data from both periods in each of the two studies will tend to have under-estimated the overall treatment effect.

Blinding of participants and clinicians to group allocation did not occur in any of the included studies. The impact of not blinding participants is that the effect size of the intervention may be over-estimated, mainly due to non-specific placebo effect[50]. This issue is compounded by the subjective nature of the primary outcome measures, the physical characteristic of the intervention[51], therapist involvement in its delivery[50], and the context of chronic condition and chronic pain[52]. Study design elements which could minimise risk of performance and detection bias, that were not applied in the included trials are: blinding participants to the research hypothesis, ensuring equal treatment across groups (number

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and duration of sessions, quantity and quality of participant materials) , and cluster randomisation e.g. by therapist[48, 53].

The ability to detect an effect for splints, or between types of splints may be enhanced by implementing standardised 'usual care' across groups and employing strategies to promote and identify adherence[52, 53], all of which were under-utilised in the studies included in this review. However, in the included studies participant drop out was low, strengthening the statistical power and validity of study findings, and suggesting that long-term follow up (> 1 year) is feasible.

While a core set of outcome domains for investigating interventions for hand OA has been recommended (pain, physical function, HR-QoL, joint activity, and hand strength)[54], it was apparent from the multiple different outcomes measures used by studies in this review that there is no consensus about which specific tools are best suited. Further, no studies included in the current review reported HR-QoL, and several of the measures used to assess function were those which face criticism for being outmoded[55]. Outcomes that differentiate thumb CMC from hand OA are likely to better detect change where interventions target thumb CMC OA, but no 'gold standard' is currently available.

The studies included in this systematic review were lacking in demographic information about participant ethnicity, body mass index and co-morbidity, as well as additional disease characteristics. Imaging, where used, was poorly described. Entry criteria were highly variable, reflecting the lack of specific classification criteria for thumb CMC OA.

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Conclusions

The current review supports the conclusion that splinting has medium to large effects for pain and small to medium effects for function in the medium-term, and further supports the conditional recommendation of international guidelines that splinting is an effective intervention for thumb CMC OA. Current evidence, however, derives from a small number of studies with small sample sizes and short periods of follow up. Thus, the overall quality of the existing evidence is low, and it is not possible to draw firm conclusions as to the effectiveness of splinting as an intervention. Significant challenges for future studies are the lack of diagnostic criteria and the absence of a gold standard outcome measure for thumb CMC OA. Future research into the effectiveness of splinting for thumb CMC OA should ensure that appropriate sample size requirements are met, usual-care is standardised, study design is appropriate, and follow-up extends beyond one year.

Author contributions

All authors contributed to critical revision of the article and final approval. Miranda Buhler, Cathy Chapple, Simon Stebbings and David Baxter contributed to the conception and design of the study, and analysis and interpretation of the data. Miranda Buhler and Bahram Sangelaji contributed to acquisition of data.

Miranda Buhler (Miranda.Buhler@postgrad.otago.ac.nz) takes responsibility for the integrity of the work as a whole.

Competing interest statement

None of the authors have competing interests

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Figure legends

Figure 1. Flowchart of study selection process

Figure 2. Risk of bias graph: summary of each risk of bias item presented as percentages across all included studies.

Figure 3. Forest plot: effectiveness of splint versus no splint for pain and function forest plot, at short-term (0-3 months) and medium-term (3-12 months).

Figure 4. Forest plot: effectiveness of splint versus no splint for pain and function forest plot, at short-term (0-3 months) (studies with low risk of selection bias).

Figure 5. Forest plot: effectiveness of soft versus rigid splint for pain and function at short-term (0-3 months), and MCP included versus MCP not included splint for pain and function at short-term (0-3 months) and medium-term (3-12 months).

Figure 6. Forest plot: effectiveness of soft versus rigid splint for pain and function, and MCP included versus MCP not included splint for pain and function, at short-term (0-3 months) (studies with low risk of selection bias).

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546 **Table 1.** Characteristics of the studies selected for inclusion

First author, year, country	**Study purpose (setting)**	**Study design N allocated (N analysed)**	**Outcomes**	**Time points**	**Population**		
					Entry criteria (actual disease severity and duration, mean ± SD years*)	Baseline pain and function, mean ± SD*	Age, mean ± SD years (women, %)
Arazpour 2017, Iran	Compare splint vs no splint: rigid CMC splint, provider NA, *"Wear during ADLS, remove when sleeping"* for 4 weeks; control – usual medical care. (University hospital orthopaedic clinic)	Randomised controlled parallel 25 (25)	Pain: on using pen (splint group) or average in last week (control) (VAS, 0-10) Function: (MHQ, 0-100)	0, 4 weeks	Clinical criteria, radiographic criteria (grade I or II) (symptoms 13.08 ± 2.39)	4.48 ± 1.55† 58.58 ± 15.22†	50.95 ± 5.92 (87.36)
Becker 2013, United States	Compare soft CMC/MCP splint vs rigid CMC/MCP splint: both provided by study-trained occupational therapist, *"Wear whenever symptoms day or night"* for 5-15 weeks. (Tertiary hospital outpatient clinic)	Randomised controlled parallel 119 (62)	Pain (ordinal scale, 0-10) Function (DASH, 0-100)	0, 5-15 weeks	Clinical criteria (NA)	5.0 ± 2.19 28.18 ± 17.23	63 ± 8.1 (77.4)

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Cantero-Tellez 2017, Spain	Compare rigid CMC/MCP splint vs rigid CMC splint: provided by hand therapy clinician experienced in orthopaedic cases, *"Use orthosis during the nighttime and also during daytime ADL for 3 to 4 hours per day"*, for 3 months. (Hand centre clinic)	Randomised controlled parallel 66 (66)	Pain on activity (VAS, 0-100) Function (QuickDASH, 0-100)	0, 1 week	Clinical criteria, pain VAS >40/100, radiographic criteria (Eaton-Littler grade II or III) (NA)	77 ± 7.5†‡ 40.95 ± 6.84†‡	63.75 ± 9.55 (83.33)
Cantero-Tellez 2018, Spain	Compare rigid CMC/MCP splint vs rigid CMC splint: both provided by experienced hand therapy clinician, *"Use during the night & during daytime activities of daily living for 3-4 hours"*, 3 months. (Hand rehabilitation clinic)	Quasi-randomised controlled parallel 84 (84)	Pain on activity (VAS, 0-100) Function (DASH, 0-100)	0, 3 months	Clinical & radiographic criteria (NA)	76.91 ± 10.84† 50.12 ± 6.46†	63.95 ± 9.3 (91.7)
Gomes Carreira 2010, Brazil	Compare splint vs no splint: rigid CMC/MCP provided by occupational rheumatology specialist, *"Wear during activity only"*, for 3 months; control – usual care. (NA)	Randomised controlled parallel 40 (40)	Pain in last week, when splint is off (VAS, 0-10) Function (DASH, 0-100)	0, 45 days, 3 months	ACR clinical criteria, pain VAS 3≤7, ACR radiographic criteria (Grade II 97.5%, 7 ± 4.9)	5.1 ± 1.24† 40.55 ± 17.5†	63.95 ± 9.3 (100)

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Hermann 2014, Norway	Compare splint vs no splint: soft CMC/MCP/wrist splint, provider NA, *"Wear whenever symptoms day or night"*, + exercises + usual medical care, 2 months; control – exercises + usual medical care. (Hospital rheumatology department)	Randomised controlled parallel 59 (55)	Pain (right hand) (NRS, 0-10) Function (AUSCAN function subscale, 1-5)	0, 2 months	ACR hand OA clinical criteria, pain on palpation CMC joint (15.2, range 5 – 41)	Median 4 (0, 9) Median 4.8 (1.9)§	70.5 ± 6.7 (98.3)
McKee 2006, Canada	Compare rigid CMC/MCP vs rigid CMC splint: both provided by study-trained therapist, *"Wear whenever symptoms day or night"*, 4 weeks. (Hand therapy, physiotherapy, occupational therapy clinic)	Non-randomised controlled parallel 27 (20)	Pain (PRWHE pain subscale, 0-50) Function (PRWHE function subscale, 0-50)	0, 4 weeks	Clinical criteria +/- radiographic criteria (NA)	28.09 ± 8.52†‖ 38.13 ± 19.79†‖	59 ± 7.1 (87)
Rannou 2009, France	Compare splint vs no splint: rigid CMC/MCP/wrist splint provided by study-trained occupational therapist, *"Wear at night only"*, + usual medical care, 1 year; control – usual medical care. (Hospital or private	Randomised controlled parallel 112 (101)	Pain in previous 48 hours (VAS, 0-100) Function (Cochin, 0-90)	0, 1 month, 1 year	Clinical criteria, radiographic criteria – Kallman (1.41 ± 2.07)	46.52 ± 19.5† 18.73 ± 12.63†	63.25 ± 7.72 (90.18)

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	rheumatology clinic)						
Sillem 2011, Canada	Soft CMC/MCP/wrist splint vs rigid CMC splint: both provided by study-trained therapist, *"Wear whenever symptoms day or night"*, 4 weeks. (Outpatient hand therapy departments – 3 sites)	Randomised controlled cross-over 56 (56)	Pain (AUSCAN pain subscale, 0-50) Function (AUSCAN function subscale, 0-90)	0, 4 weeks	Clinical criteria (2.99 ± 4.68)	27.76 (SD NA)† 52.88 (SD NA)†	64.05 ± 8.61 (91)
Van der Vegt 2017, Netherlands	Rigid CMC/MCP splint vs semi-rigid CMC splint: both provided by 1 of 14 study-trained experienced hand therapy clinicians, instructions NA, 2 weeks. (Hospital and medical centre orthopaedic, plastics, rheumatology and hand therapy clinics – 3 sites)	Randomised controlled cross-over 63 (59)	Pain recorded in daily dairy over 3 days (VAS, 0-10) Function (FIHOA, 0-30)	0, 2 weeks	Clinical criteria, radiographic criteria – Eaton-Glickel (Grade I or II 43%; grade III or IV 57%, >1 year 49%)	3.7 ± 2.05† 9.65 ± 6.03†	60.1 ± 8.2 (70)
Weiss 2000, United States	Rigid CMC/MCP/wrist splint vs rigid CMC splint: both provided by study-trained certified hand therapist, *"Wear whenever symptoms day or night"*, 1 week. (Hand clinic)	Randomised controlled cross-over 26 (26)	Pain currently, after functional use (VAS, 0-10) Function (pinch grip strength, Kg)	0, 1 week	Clinical criteria, radiographic criteria – Eaton-Littler (<6 months to >5)	6.23 ± 2.01‖ 3.30 ± 1.02‖	57, range 36 – 88 (81)

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Weiss 2004, United States	Soft CMC/MCP splint vs rigid CMC splint: provider NA, *"Wear whenever symptoms day or night"*, 1 week. (Hand clinic)	Randomised controlled cross-over 25 (25)	Pain currently, after functional use (VAS, 0-10) Function (pinch grip strength, Kg)	0, 1 week	Radiographic criteria – Eaton-Littler stage I or II +/- clinical criteria (Grade I or II, <6 months up to 5 years)	5.42 ± 2.4 3.40 ± 1.8	NA (84)

CMC: carpometacarpal joint; NA: not available; VAS: visual analogue scale; MHQ: Michigan Hand Questionnaire; MCP: metacarpophalangeal joint; DASH: Disabilities of Arm, Shoulder, Hand questionnaire; NS: not specified; QuickDASH: Quick Disabilities of Arm, Shoulder, Hand questionnaire; ACR: American College of Rheumatology; AUSCAN: Australian Canadian Osteoarthritis Hand Index; PRWHE: Patient-Wrist and Hand Evaluation; FIHOA: Functional Index for Hand Osteoarthritis; Kg: kilogram

* Unless otherwise stated† Values calculated from group-level data for study-level means and SD using a freely available online software (https://www.statstodo.com/CombineMeansSDs_Pgm.php)

‡ Data extracted from table II only, in Cantero-Tellez 2017

§ Unpublished data

|| Data extracted from graph

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548 **Table 2**. Summary of results of included studies

First author, year	Outcome	Time point	Change in score (mean ± SD)*	Mean difference (95% CI)
Arazpour 2017	Pain	Short-term	Rigid CMC splint: -1.0 ± 1.99	-0.48 (-1.31, 0.35)
			Control group: 0.11 ± 1.34	
	Function	Short-term	Rigid CMC splint: 0.85 ± 20.20	4.96 (-10.40, 20.32)
			Control group: -4.11 ± 17.98	
Becker 2013	Pain	Short-term	Soft CMC/MCP splint: -0.81 ± 2.9	0.09 (-1.4, 1.2)
			Rigid CMC/MCP splint: -0.9 ± 2.2	
	Function	Short-term	Soft CMC/MCP splint: - 2.5 ± 17.4	1.3 (-9.8, 5.9)
			Rigid CMC/MCP splint: -3.8 ± 13.2	
Cantero-Tellez 2017	Pain	Short-term	Rigid CMC/MCP splint: -31 ± 1.8†	-2 (-2.87, -1.13)
			Rigid CMC splint: -29 ± 1.8†	
	Function	Short-term	Rigid CMC/MCP splint: -4.1 ± 0.8†	1.9 (1.51, 2.29)
			Rigid CMC splint: -6.0 ± 0.8†	
Cantero-Tellez 2018	Pain	Medium-term	Rigid CMC/MCP splint: -25.6 ± 1.7	0.6 (-1.35, 0.15)‡
			Rigid CMC splint: -25.0 ± 1.8	
	Function	Medium-term	Rigid CMC/MCPsplint: -10.3 ± 1.0	1.7 (1.27, 2.13)‡
			Rigid CMC splint: -12.0 ± 1.0	
Gomes Carreira 2010	Pain	Short-term	Rigid CMC/MCP splint: -2.0 ± 2.37	1.7 (3.17, 0.23)‡
			Control group: -0.3 ± 2.36	
		Medium-term	Rigid CMC/MCP splint: -2.2 ± 2.46	2.3 (3.82, 0.78)‡
			Control group: 0.1 ± 2.44	
	Function	Short-term	Rigid CMC/MCP splint: -7.3 ± 24.40	0.3 (7.56, -14.53)‡
			Control group: -7.6 ± 23.43	
		Medium-term	Rigid CMC/MCP splint: -10.5 ± 24.69	3.8 (-18.48, 10.88)‡

			Control group: -6.7 ± 22.65	
Hermann 2014	Pain	Short-term	Soft CMC/MCP splint: -0.3 ± 2.56	0.09 (-1.2, 1.4)
			Control group: -0.2 ± 2.98	
	Function	Short-term	Soft CMC/MCP splint: -0.2 ± 1.29[§]	0.06 (-0.7, 0.8)[§]
			Control group: -0.3 ± 1.26[§]	
McKee 2006	Pain	Short-term	Rigid CMC/MCP splint: -10.24 ± 12.47[‖]	2.8 (-8.19, 13.69)‡
			Rigid CMC splint: -12.99 ± 11.77[‖]	
	Function	Short-term	Rigid CMC/MCP splint: -7.13 ± 23.34[‖]	11.3 (-11.33, 33.97)‡
			Rigid CMC splint: -18.45 ± 28.11[‖]	
Rannou 2009	Pain	Short-term	Rigid CMC/MCP splint: -10.1 ± 22.25	0.6 (-7.9, 9.1)
			Control group: -10.7 ± 22.38	
		Medium-term	Rigid CMC/MCP splint: -22.2 ± 23.08	-14.3 (-23.0, -5.2)
			Control group: -7.9 ± 23.48	
	Function	Short-term	Rigid CMC/MCP splint: 1.3 ± 10.29	1.6 (-2.3, 5.5)
			Control group: -0.3 ± 10.29	
		Medium-term	Rigid CMC/MCP splint: -1.9 ± 11.20	6.3 (-10.9, 1.7)
			Control group: 4.3 ± 11.53	
Sillem 2011	Pain	Short-term	Soft CMC/MCP splint: -2.05 ± 9.54	3.7 (0.68, 6.76)
			Rigid CMC splint: -5.69 ± 11.08	
	Function	Short-term	Soft CMC/MCP splint: -2.69 ± 16.33	3.1 (-1.12, 7.38)
			Rigid CMC splint: -5.54 ± 17.37	
Van der Vegt	Pain	Short-term	Rigid CMC/MCP splint: -0.3 ± 2.97	0.0 (-1.05, 1.05)‡
2017			Semi-rigid CMC splint: -0.3 ± 2.83	
	Function	Short-term	Rigid CMC/MCP splint: 0.0 ± 8.56	0.9 (-2.15, 3.95)‡
			Semi-rigid CMC splint: -0.9 ± 8.34	

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Weiss 2000	Pain	Short-term	Rigid CMC/MCP: -2.65 ± 2.88[II]	0.4 (-2.16, 1.40)‡
			Rigid CMC splint: -2.27 ± 3.62[II]	
	Function	Short-term	Rigid CMC/MCP splint: 0.25 ± 1.67[II]	0.3 (-0.61, 1.25)‡
			Rigid CMC splint: -0.07 ± 1.75[II]	
Weiss 2004	Pain	Short-term	Soft CMC/MCP splint: -3.13 ± 2.91	-1.3 (-3.01, 0.41)‡
			Rigid CMC splint: -1.83 ± 3.26	
	Function	Short-term	Soft CMC/MCP splint: -0.3 ± 2.55	0.0 (-1.39, 1.39)‡
			Rigid CMC splint: 0.3 ± 2.48	

CMC: carpometacarpal joint; **MCP:** metacarpophalangeal joint

* Negative value indicates improvement

† Data extracted from table II only, in Cantero-Tellez 2017

‡ Calculated in RevMan

§ Unpublished data

[II] Data extracted from graph

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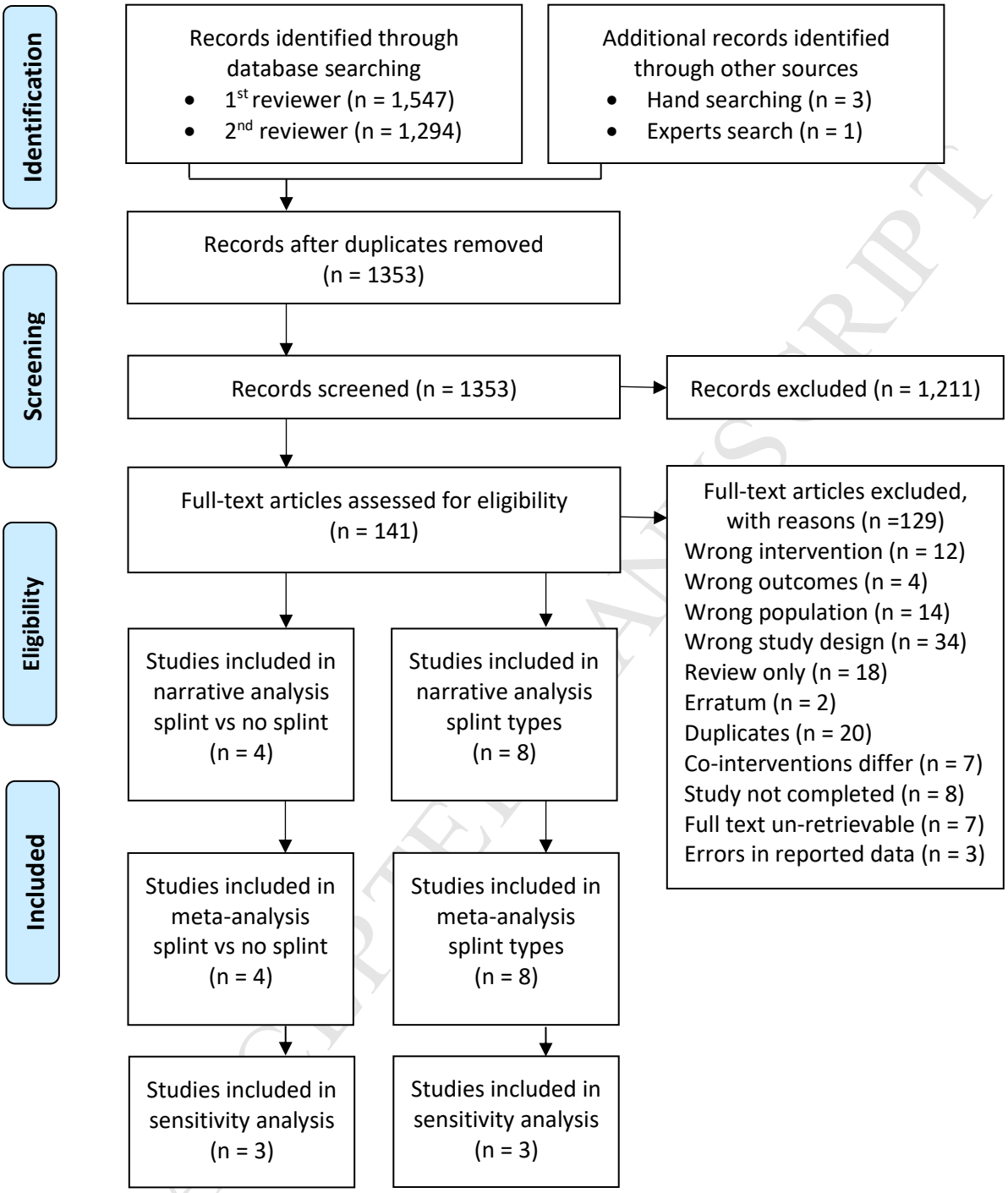
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Screening
Eligibility
Included
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• 2nd reviewer (n = 1,294)
Additional records identified through other sources
• Hand searching (n = 3)
• Experts search (n = 1)
Records after duplicates removed (n = 1353)
Records screened (n = 1353)
Records excluded (n = 1,211)
Full-text articles assessed for eligibility (n = 141)
Full-text articles excluded, with reasons (n =129)
Wrong intervention (n = 12)
Wrong outcomes (n = 4)
Wrong population (n = 14)
Wrong study design (n = 34)
Review only (n = 18)
Erratum (n = 2)
Duplicates (n = 20)
Co-interventions differ (n = 7)
Study not completed (n = 8)
Full text un-retrievable (n = 7)
Errors in reported data (n = 3)
Studies included in narrative analysis splint vs no splint (n = 4)
Studies included in narrative analysis splint types (n = 8)
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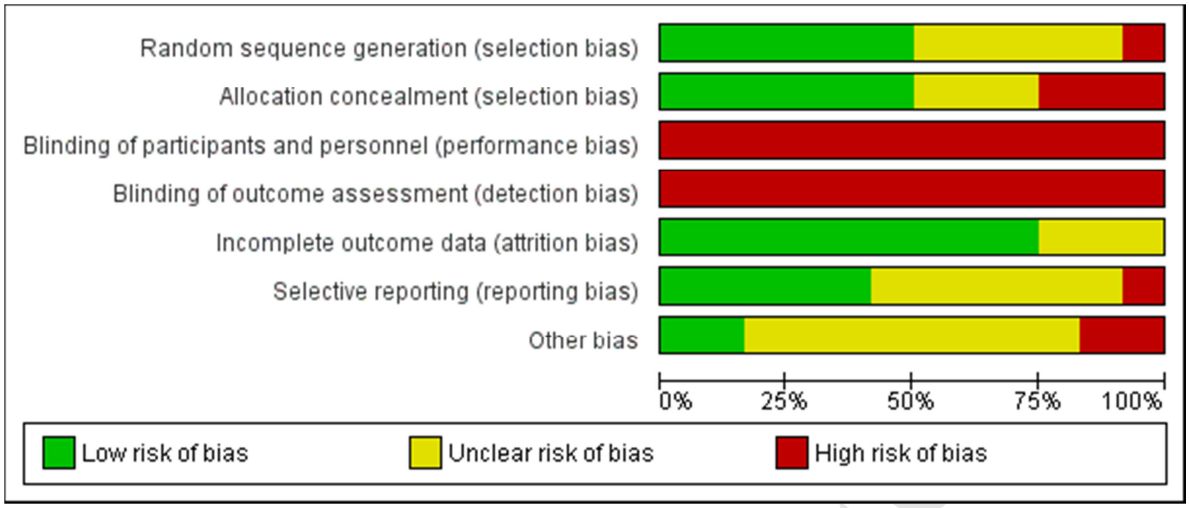

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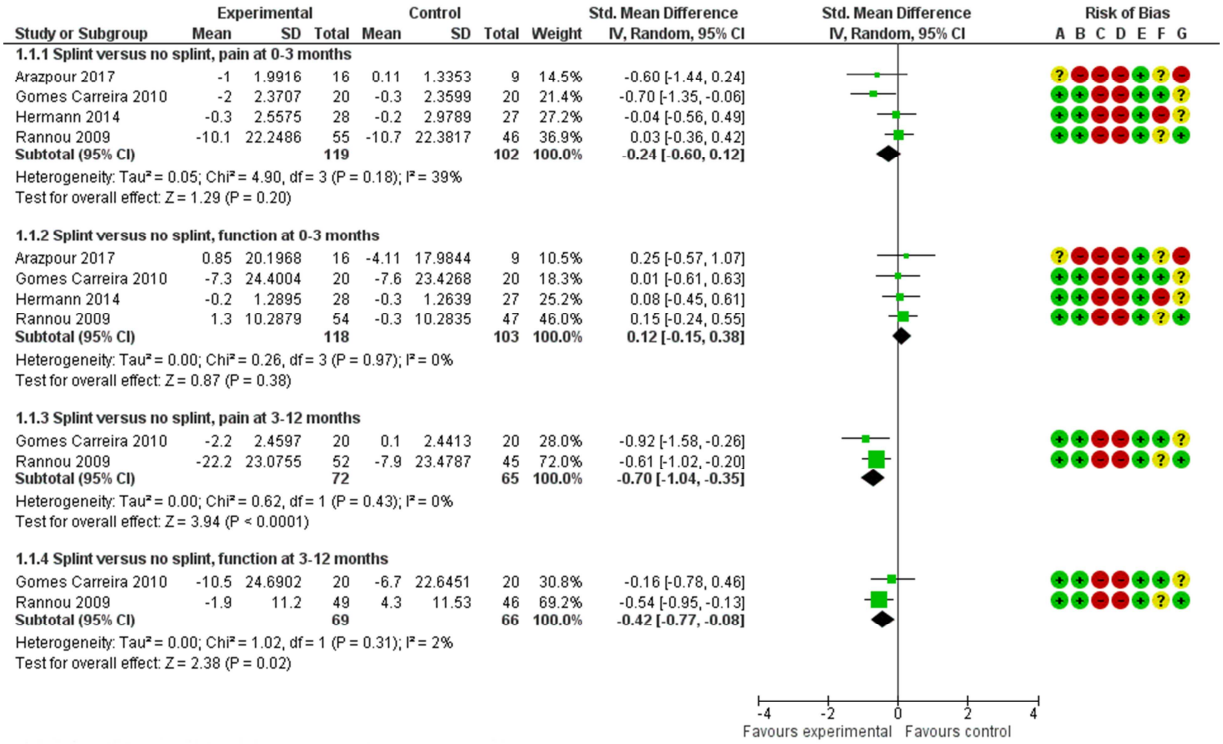

Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective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

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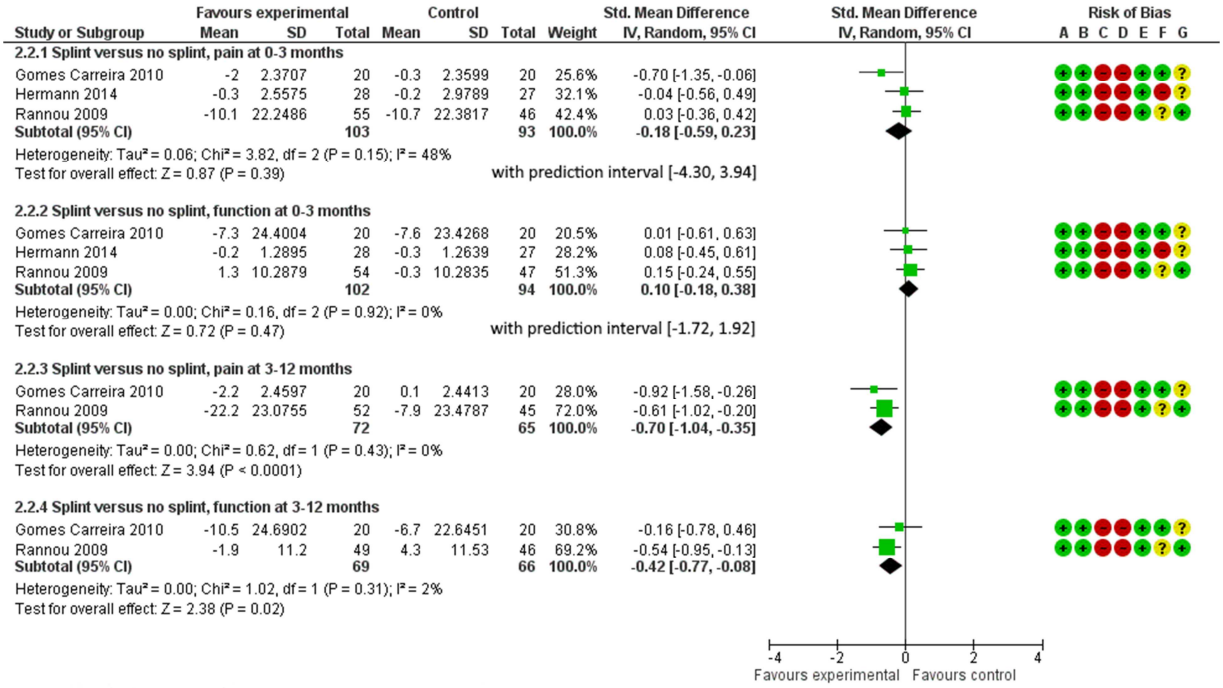

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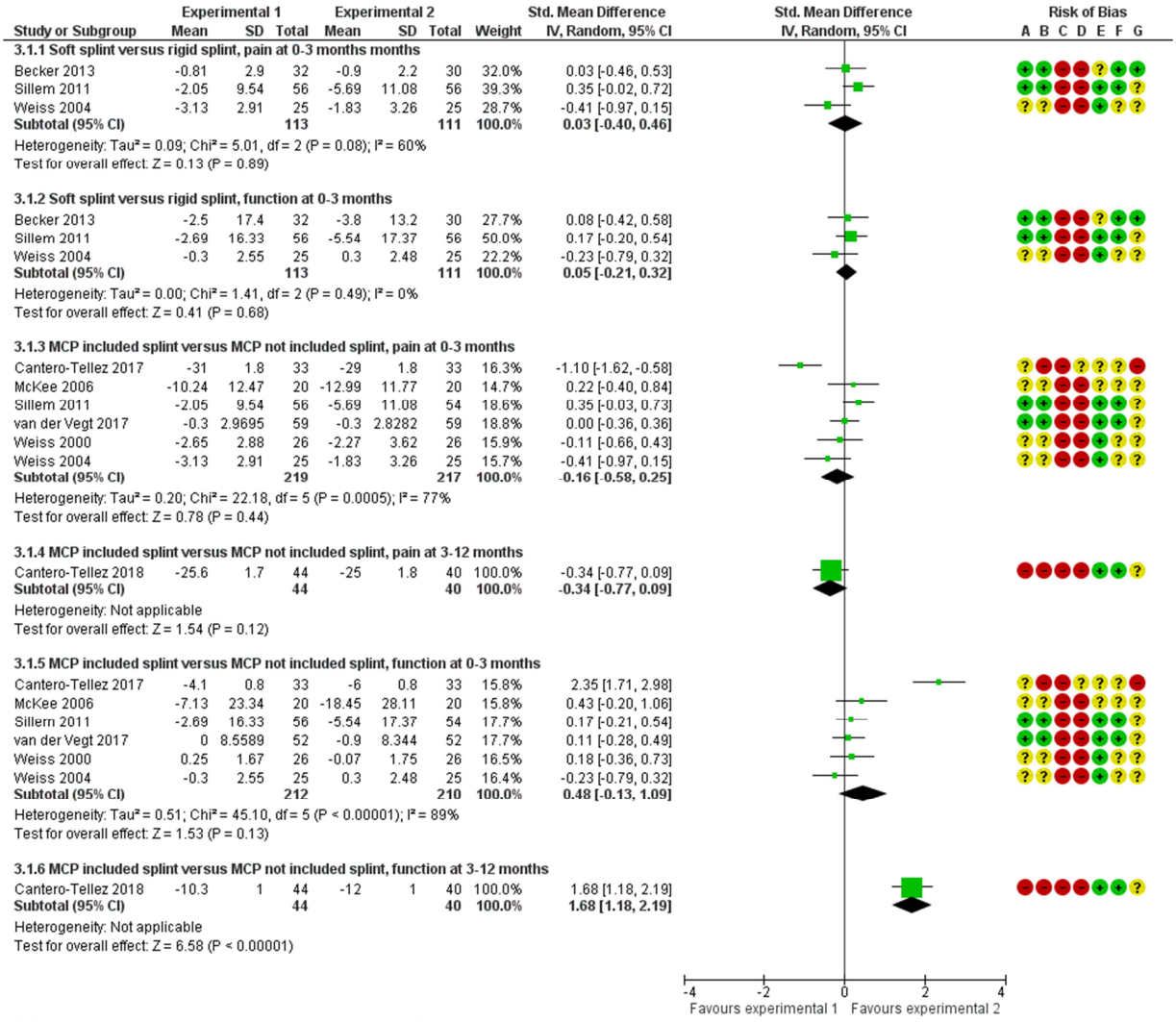

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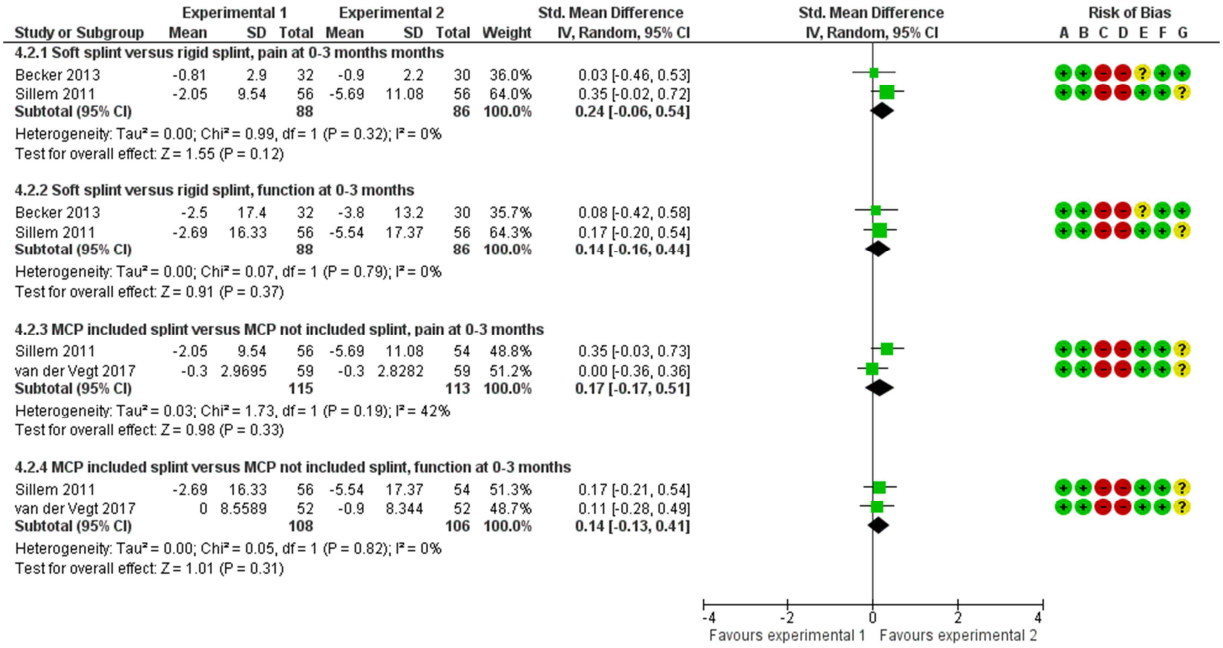
(**F**) Selective reporting (reporting bias)
(**G**) Other bias



Risk of bias legend

(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

ACCEPTED MANUSCRIPT