Overall Effects and Moderators of Rehabilitation in Patients with Wrist Fracture: A Systematic Review

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Abstract

Background & Aims: Wrist fractures constitute the most frequently occurring upper limb fracture. Many patients report persistent pain and functional limitations up to 18 months following wrist fracture. Identifying which patients are likely to gain the greatest benefit from rehabilitative treatment is an important research priority. This systematic review aimed to summarise effectiveness of rehabilitation after wrist fracture for pain and functional outcomes and identify potential effect moderators of rehabilitation.

Methods: A comprehensive search of seven databases (including MEDLINE, EMBASE, and PEDRO) was performed for randomised controlled trials involving adults >50years who sustained wrist fracture, and received one or more conservative treatments (e.g., exercise/manual therapy, lifestyle, diet or other advice). Study selection, data extraction and risk of bias assessment were conducted independently by two reviewers. Results of included trials were summarised in a narrative synthesis.

Results: 3225 titles were screened and 21 studies satisfying all eligibility criteria were reviewed. Over half of included studies (n=12) comprised physiotherapy and/or occupational therapy interventions. Rehabilitative exercise/manual therapy was generally found to improve function and reduce pain up to 1 year after wrist fracture. However, effects were small, and home exercises were found to be comparable to physiotherapist-led exercise therapy. Evidence for the effects of other non-exercise therapy (including electrotherapy, whirlpool) was equivocal and limited to the short-term (<3months). Only 2 studies explored potential moderators and did not show evidence of moderation by age, sex, or patient attitude of the effects of rehabilitation.

Conclusion: Effectiveness of current rehabilitation protocols after wrist fracture is limited; and evidence for effect moderators is lacking. Currently available trials are not large enough to produce data on sub-group effects with sufficient precision. To aid clinical practice and optimise effects of rehabilitation after wrist fracture, potential moderators need to be investigated in large trials or meta-analysis using individual participant data.

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Key words: Wrist fracture, distal radial fracture, rehabilitation, exercise therapy, moderators

Impact statement

Many patients report persistent pain and functional limitations up to 18 months following wrist fracture. Effectiveness of current rehabilitation protocols after wrist fracture is limited and may be due to insufficient targeting of specific rehabilitation to patients who are likely to benefit most. However, evidence for effect moderators is lacking within currently available literature. To aid clinical practice and optimise effects of rehabilitation, investigating potential moderators of rehabilitation in patients with wrist fracture via large trials or meta-analysis of individual participant data is research and policy imperative.

Background

Fractures of the wrist account for 25% of all fractures in the UK[1,2] and result in a five-fold increase in healthcare utilisation and associated expenditures in the year post fracture.[3] In terms of disease burden, 63% of people with upper limb fracture report ongoing pain six months post fracture, and up to 15% develop complications such as persistent neuropathies, long-term impairment, and complex regional pain syndrome.[4-6]

In adults aged over 50, wrist fractures are likely to represent a fragility fracture, defined as fractures which occur following an episode of low trauma.[7,8] Such fractures are often the first indicator of poor bone health and are associated with debilitating consequences with respect to activities of daily living such as work, driving, mobility, and self-care, leading to: loss of independence; re-fracture at other sites; reduced quality of life; increased health and social care consumption; and up to a 14% increase in mortality rates seven years post-fracture.[5,6,9-13]

Fragility wrist fractures may also be an early signal in the life course of a middle to older aged adult, indicating the potential for a cascade of further adverse events (e.g., falls, other fragility fractures, frailty, multi-morbidity, and polypharmacy). As such, fragility wrist fractures are a key target for early rehabilitation, whilst the potential for rehabilitation is at its maximum.

Treatment of wrist fractures include surgical and non-surgical (conservative) approaches.[14] Clinical decision making regarding the balance of potential harms and benefits of different treatment options usually varies depending on the patient.[14] Regardless of the treatment chosen, rehabilitation is a core component of a post-fracture care plan and may involve any or all of the following: occupational therapy (OT); education and advice; diet and lifestyle interventions; pharmacy review; falls prevention; exercise therapy; and a variety of splinting devices and electro/magnetic therapies.[15]

However, within currently available literature, the observed effect sizes for reducing pain and improving function following wrist fracture are mostly small and highly imprecise.[3,14,16] Findings of less-than-optimal effectiveness of rehabilitation post wrist fracture may result from insufficient targeting of rehabilitation to patients with wrist fractures who are likely to benefit most. Concerns about the effectiveness and generalisability of existing treatments for post wrist fracture rehabilitation exist because of varying rehabilitation protocols, and different patient profiles. The degree to which rehabilitative treatments match the needs of patients with wrist fracture is germane to clinical decision making and to optimise efficacy of care. Identification of key characteristics of optimal rehabilitative treatment protocols (including therapy utilisation, timing, duration, and technique), and understanding of moderating factors are imperative for the development of effective patient-centred wrist fracture rehabilitation protocols. Moderators are factors that affect the direction and/or strength of treatment effect, and may include patient characteristics, such as age, sex, lifestyle, characteristics of the fracture, or comorbidity.[13]

This systematic review therefore aims to summarise evidence for:

a) The overall effects of rehabilitative treatments for patients with wrist fracture.

b) Potential moderators (predictors) of the effects of treatments for patients with wrist fracture.

Methods

Protocol/protocol registration: This systematic review was written using the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidance statement.[17] The review also aligns with the Synthesis without meta-analysis (SWiM) in systematic reviews reporting guideline.[18] A full protocol was established for this study and was registered a priori on the international prospective register of systematic reviews (Prospero ID: CRD4201810776).

Information sources and search strategy: A comprehensive search strategy was developed by an information specialist as part of the review team which included clinicians, physiotherapists, and academics with subject knowledge of wrist fracture and osteoporosis. A search of the following electronic databases was conducted from their inception until April 2020: Medline, EMBASE, CINAHL, AMED, Cochrane Central Register of Controlled Trials [CENTRAL], and Web of Science. (*see appendix for full search strategy*). Database searches were supplemented by hand searching bibliographies of eligible articles and other relevant literature in the field to identify additional studies and grey literature.

Study selection and eligibility: The review process was managed using the Covidence software package (https://www.covidence.org). Using pre-defined eligibility criteria, two independent reviewers screened the titles and abstracts of retrieved citations. Conflicts were resolved with discussion or by the independent opinion of a third reviewer. Studies progressing to full-text stage were similarly screened. The following criteria were used to assess eligibility of each trial to be included in the review:

a) *Participants*: Adults (~ 50 years of age and over) with history of wrist fracture. As many trials included participants from a wider age range, we considered trials that reported a mean age -1 SD (standard deviation) totalling >45, to ensure the majority of participants in eligible trials were 50 years or older.

b) *Interventions/exposures*: Any conservative (non-surgical) treatment including any of the following: diet and exercise, falls prevention, OT, exercise therapy, acupuncture, and electromagnetic therapies. NB: Primary studies focusing on pharmaceutical and/or nutraceutical treatments only were excluded from this review.

c) *Comparisons or control arms*: Control group including placebo, no intervention, or comparison with other conservative interventions.

d) *Outcomes of interest*: Primary outcome of interest was pain and functional disability following wrist fracture. Secondary outcomes included post-treatment complications, quality of life, healthcare utilisation, and work absence.

e) *Study design*: Only randomised control trials (RCTs) were included. (NB: RCTs were required for moderation analysis, therefore no other study types considered).

Data extraction: Eligible full texts were subjected to data extraction using a pilot tested data extraction form, customised for this review. The aim(s), rationale, design, study setting, inclusion and exclusion criteria for each of the eligible studies were documented. Study-level data were also collected on participant characteristics including details of treatments received (type, duration, intensity, and frequency of sessions); concurrent intervention (where reported); treatment uptake; outcome measures; treatment outcomes; follow-up time points; potential predictors of treatment effect; and complications. Data regarding the use of subgroup or moderation analysis including estimates of subgroup effects or associations between potential predictors and treatment effects were also sought from included studies. Full data extraction was conducted for all included studies by one reviewer and was checked by an independent second reviewer to ensure validity and consistency of extracted data.

Risk of bias assessment: Two independent reviewers assessed eligible full texts based on the Cochrane Risk of Bias tool.[19] Reviewers were blinded to the responses from the other reviewer until both reviewers had completed their reviews. Disagreements were resolved with discussion.

Methodological quality of moderation analysis: Assessment of the quality of moderation analysis was based on existing quality criteria, outlined by Pincus et al. (2011), which provide an estimation of the level of moderation evidence.[20] The five criteria considered when making a judgement on the overall level of evidence for moderation include an a priori hypothesis, presence of a theory or evidence-based selection of moderators to be tested, measurement of moderators prior to randomisation, quality of measurement of baseline factors, and an explicit test of the effect of interaction between moderator and treatment on outcome. Each criterion is scored as either met or not met, resulting in a total score ranging from 0-5. A maximum score of five out of five allows findings to be regarded as confirmatory evidence, while the presence of three criteria allow findings to be regarded as exploratory evidence.[19]

Data analysis and synthesis: Statistical pooling of data (via random effects meta-analysis) was not possible as planned because of the substantial differences in patient population, settings, interventions, and outcomes used. This systematic review therefore followed a narrative approach.[19,20] Synthesis involved an initial description of the characteristics of the included studies and their risk of bias. Included studies were subsequently grouped into broad categories by intervention type (e.g., exercise/manual therapy as part of physiotherapy (PT) or OT; other non-exercise therapy including acupuncture, electrotherapy, aids/orthotics), and results reported in relation to review outcomes (i.e., pain and functional disability). A summary of evidence from studies which included analysis of, or suggested moderators of treatment outcomes, was then undertaken. For this, studies were categorised into two groups: (i) studies with further analysis of between-arm treatment effect for patient subgroups (or formal moderation analysis) and (ii) studies that suggested potential moderators of treatment effect without formal analyses.[21]

Results

In the subsequent paragraphs, a description of all included studies, including risk of bias and treatment effects (grouped by intervention type), is given first. This is followed by a description of the moderators highlighted in the body of evidence and an evaluation of the level of evidence for moderators of treatment effect.

Characteristics of included studies

Details of the study identification and selection process is illustrated in Fig 1. After removing duplicates (n=3216), our search strategy yielded 3550 unique titles which were screened. Of these, 3225 were found to be irrelevant during title and abstract review. A total of 325 studies qualified for full-text review, and 21 of these fully met pre-specified eligibility criteria and were included in the final review. Reasons for exclusion of full-text articles included paediatric patient population, surgical interventions, irrelevant outcomes (e.g., radiological) and non-randomised study designs.

Included studies were published over a period of 34 years between 1986 and 2020.[22-24] Studies were conducted across Europe[9,25-32], North America[22,33,34], South America[35], Asia[36,37,41], and Australia.[23,38-40] All of the studies were conducted in the primary care/ community sector (though this was not part of our inclusion criteria). A total of 1065 participants with a mean age of 57.8 years and range from 49.9 (SD 10.15) to 75.85 (SD 7.65) years were included in this review.[27,38] Sample sizes of included studies ranged from 18 to 119.[26,38] On average, study samples consisted of a greater proportion of females compared to males: [mean proportion of females was 75.9 %; this ranged from 34% to 100%[26,28]]. One study did not give data on sex.[23] In terms of fracture types and severity, most studies did not specify or report fracture classifications but where reported, fracture severity was variable. Included studies recruited patients with DRFs (n=16), two studies recruited people with Colle's fractures while the rest included mixed population involving different types of fractures at the wrist. The characteristics of included studies are summarised in Table 1.

Risk of Bias: Of the 21 studies included, only two were assessed as having low risk of bias in all domains of risk assessment, which were also the only two studies assessed as having low risk of bias in relation to blinding of participants and personnel.[23,34] This domain also had the highest number of studies (n=13) assessed as having unclear risk of bias due to insufficient information to adequately assess risk.[22,25–27,29,31,32,35,37–41] Though fourteen studies had a low risk of selective reporting of outcomes, this domain also accounted for the highest number of studies (n=6) having a high risk of bias. Reasons contributing to other sources of bias in included studies were deviation from protocol[41], not presenting data on baseline characteristics[23], not clearly stating how patients were recruited[28] and selective presentation of significant outcomes.[25,28,31,33,37,38] Summary of risk of bias for each included study is presented in Fig 2.

Outcome Measures

Pain and function were the primary outcomes for this systematic review, although included studies also investigated secondary outcomes of interest: post-treatment complications (n=6), quality of life (n=3), healthcare utilisation (n=0), and work absence (n=2). The Patient Related Wrist Evaluation Score (PRWE) was the most commonly used outcome measure to assess pain, function, and difficulty performing everyday activities.[24,26,27,30,33–36,39,40] Other measures used to assess pain were the Visual Analogue Scale (VAS),[23,24,26,30,35] and the present pain intensity score (PPI).[22] In terms of function, the Disabilities of the Arm, Shoulder and Hand questionnaire (DASH) or QuickDASH were often used in combination, or as an alternative, to PRWE for investigating the level of functional disability in performing everyday activities.[9,23,24,26,27,35] Other outcome measures used to assess function were the Werley functional score[25] encompassing pain, disability, ROM and radiography,[23] and the Michigan Hand questionnaire (MHQ), which investigates pain, function, satisfaction and activities of daily living.[27]

Effectiveness of conservative treatments following wrist fracture.

Table 2 presents a summary of results for studies reporting pain and function outcomes of conservative treatments post wrist fracture.

1. Exercise /manual therapy as part of PT or OT

Interventions: Sixteen studies[9,23–26,28–31,33-35,38–41] investigated exercise as part of PT/OT-led interventions. OT exercises included hand strengthening and function focused programmes[23,25]. In addition to localised rehabilitation of the hand affected by wrist fracture, PT-led exercise intervention studies also focussed on the impact of the onset of rehabilitation [early versus late mobilisation[24,26,30,41]] and mode of delivery on treatment effectiveness. Delivery modes were mainly home-based exercise (HEP) with or without PT-led sessions versus PT-led exercise rehabilitation.[28,31,33,35,38,39] Other comparisons to PT-led exercises included the use of an advice brochure[28].

The duration of intervention ranged from 2 weeks,[29] to 52 weeks.[24] Two studies did not specify the duration of treatment for either intervention or control arms.[22,31] Frequency of therapy varied between three times a day,[39] and once a week.[23] Though over 50% of patients in treatment arms completed some form of HEP protocol (constituting up to 70% of their treatment schedule), there was no significant difference in adherence to exercise/rehabilitation protocols between control and intervention arms of studies that reported adherence.[33,41]

Effects on pain: Nine out of 16 studies assessing the effects of exercise as part of PT/OT-led interventions reported on pain outcomes.[23,24,26,28,30,31,35,39,40] Exercise was associated with reduction in pain but reported effects/differences between treatment arms were mostly limited to the short term (<6 months) and were not statistically significant.[23,24,30,31,35,39,40] Only two studies, found exercise to reduce pain symptoms for up to 1 year after wrist fractures.[26,28] There was discrepancy amongst the studies regarding any perceived advantage of PT-led exercises over HEP on pain outcomes.[26,28,30,31,39,40] Most studies reported no significant difference between either mode of delivery in the short- or long-term.[28,31,39,40] In summary, the effect of exercise on pain after wrist fracture is limited and, home exercises were found to be comparable to PT-led exercise therapy, especially when used in combination with less frequent conventional one-to-one PT-led sessions.[26,28,30,31,39,40]

Effects on function: All 16 studies reported on the effects of exercise on functional outcome after wrist fracture. Only in five studies was exercise/manual therapy as part of PT/OT rehabilitation programmes reported to lead to significant improvements in hand function compared to control.[9,23,24,30,35] For up to 1 year after commencing exercise rehabilitation for wrist fracture, most studies reported no clinically significant differences between treatment arms. Studies with longer follow-up reported worsened or no significant improvement compared to control and/or other active interventions at any given time point up to 2 years.[26,28] As with pain outcomes, there were equivocal findings with regards to the beneficial effects or added advantage of PT/OT-led exercises over HEP for functional outcomes.[22,27,32,36,37,26,28,30,31,39,40]

2. *Non-exercise interventions including acupuncture, electromagnetic therapy, others*

Interventions: Five studies[22,27,32,36,37] were identified which presented effects of non-exercise interventions; these included whirlpool therapy,[22] graded motor imagery (GMI),[27] light-therapy,[32] oedema focussed therapy involving use of compression glove,[36] and computer-regulated brush machine therapy[37] Comparisons were hot towel therapy,[22] HEP,[27] PT,[36] standard OT,[37] and standard care[32] Studies investigating these interventions differed in terms of duration (range: 2-13 weeks; most common: 2 weeks) and frequency of treatment (range: 2-10 sessions per week; most common: 2/3 sessions per week).[22,27,32,36,37] One study did not mention the duration of follow-up.[22]

Effects on pain: Four out of five studies reported pain outcomes after non-exercise/manual therapy treatments for rehabilitation of wrist fracture.[22,27,32,36] Significant effects on pain were seen for GMI, light therapy and compression gloves (after 2-, 4- and 8-weeks post-intervention),[27,32,36] but not for whirlpool therapy,[22] hot towels,[22] and computerised brush therapy[37] compared to controls. Studies trialled different treatments and controls making comparisons regarding effectiveness difficult across studies.

Effects on function: Four out of five studies assessed the effects of other non-exercise treatments after wrist fracture.[22,27,36,37] Of these, only one found no significant difference between its two treatment arms for functional outcomes.[36] Improvements in function following rehabilitation were found with GMI,[27] OT-led computer-aided brush machine,[37] and compression glove[36] compared to function in control arms. However, positive findings were associated with non-patient reported outcome measures and limited to the immediate short-term, post-intervention period (i.e., 7-15 days) indicating possible selective outcome reporting and no true clinically significant effect on functional disability after wrist fracture.[32] Functional disability as measured using grip strength was not significantly different for standard brush OT versus computer-regulated brush therapy[37] in the longer term. In summary, the effects of other non-exercise therapy for improving function following wrist fracture remains equivocal.

***Complications*:**

Of the 21 studies, 15 neither reported or investigated complications following treatment of wrist fracture as part of their trials[9,23,25,26,28,31–33,37,40] Of those remaining (n=6), reporting of onset (timing) and/or duration of symptoms of complications after wrist fracture was limited. Complex regional pain syndrome (CRPS) was the most commonly reported complications (n=4 studies) with 10-15.4% CPRS overall incidence.[23,24,26,32] Participants in the control arms of these studies were reported to be most affected by this complication, however the control arm intervention varied widely (e.g., ROM exercises, PT-led exercises, combined PT-led exercises and cryotherapy). Other listed complications included residual pain or stiffness necessitating further interventions,[26,35,39] carpal tunnel syndrome,[24] suboptimal osteosynthesis,[26] transient nerve dysfunction,[26] trigger finger,[24,26] adhesive capsulitis,[23,24,26,32] superficial wound infection,[26] Dupuytren's contracture,[26] scar problems,[26] and peripheral nerve decompression.[26] On average across studies, a 10% rate of complications (including CRPS) were reported and there was no indication of statistical difference between intervention and control arms. Incidence of complications were not reported as treatment related but studies were generally underpowered to accurately investigate the relationship between treatment effect and the incident and outcomes of complications.

Moderators of treatment effect following wrist fracture.

Two studies investigated factors assessed pre-randomisation through moderation or subgroup analysis as part of an a priori defined hypothesis regarding effect moderation.[29,37] Interventions for which moderating factors were identified included exercise therapy as part of multimodal

PT,[29] and OT with computer-regulated brush therapy.[37] Table 3a shows a summary of how these two studies performed when considered against the Pincus criteria for the identification of moderators.[20] An outline of suggested (potential) moderators and the supporting exploratory evidence base is presented in Table 3b. No study provided a methodologically valid and statistically confirmed moderation of effect for rehabilitation after wrist fracture.

Age>55, sex (female), and patient attitude towards computers were investigated as potential moderators of treatment effect. Jarus et al. investigated attitude towards computers, using appropriate statistical methods, but the results showed no significant moderation of the effect of computer-regulated brush therapy by a positive attitude towards computers.[37] Sample size however was very small (n=47 in total). The potential influence of older age was mentioned by the authors, but this was not investigated as most participants were older adults. Ratajczak et al explored the possible role of age and sex on the effectiveness of a rehabilitation package with massage (compared to no massage), using descriptive statistics to present improvement in outcomes in age and sex subgroups, and within each treatment arm.[29] Subgroup effects (between treatment arms) were not presented, and interaction was not tested. The results showed similar outcomes across all subgroups and did not provide evidence of moderation by age or sex of the effect of adding massage, but sample size is again small (n=40 in total).

Additional factors which were not formally investigated using subgroup/moderation analysis, but suggested (e.g. in the discussion section of other studies) to be potential moderators of the effect of rehabilitative interventions for wrist fracture included: e.g. functional impairment before fracture,[31] malunion at 6 weeks after fracture,[31] high level of pain at baseline comminution and joint involvement in fracture,[25,31,35] duration of immobilisation,[24,26,30,31,41] frequent falls,[28,29,32] low adherence to prescribed treatments,[28,34,39] depression,[9] and low patient expectations.[31,37,39]

Discussion

This systematic review synthesised evidence concerning the effectiveness of rehabilitation following wrist fracture. Importantly, it also aimed to summarise evidence for moderators or potential moderators of the effects of rehabilitative treatments following wrist fracture. Findings generally indicate modest improvement in patient outcomes. We found little evidence for the effectiveness of rehabilitation compared to 'usual care' control arms, as all included studies involved active treatment intervention protocols compared against each other in many different ways and combinations. Rehabilitative treatments including electromagnetic therapies and whirlpool were not shown to have a significant effect for improving pain and function following wrist fracture. Though some studies involving exercise/manual therapy as part of a PT-led intervention showed beneficial effects for pain and function, estimates were small and may not be clinically important.

The optimum time for mobilisation is yet to be determined but in studies where participants begin PT rehabilitation **as early as two weeks post-surgical reduction of fracture**, beneficial effects for function in the short- and long-term were found. Home exercises in combination with fewer supervised therapist-led sessions were found to lead to similar effects on patient outcomes compared to fully supervised, facility-based exercise rehabilitation sessions (in the short term up to 6 months). However, adherence was variable and not well reported for most studies. It is therefore important that clinicians consider how to optimise engagement and adherence when designing rehabilitative treatment protocols for wrist fracture patients.

To our knowledge, this is the first systematic review to extract and summarise evidence for moderators of the effects of conservative treatments for wrist fracture. Only two studies investigated possible effect moderation by age>55, sex (female) or patient attitude, with only one study using appropriate statistical methods, but results suggested there was no influence of these factors on the effects of rehabilitation after wrist fracture. It must be noted however that both trials were very small (less than 30 patients per intervention arm) and not powered to detect interaction. Variation in the effects of rehabilitative treatments following wrist fracture are possibly dependent on a wider range of factors which have yet to be investigated formally in sufficiently powered randomised trials. Earlier reports in this field[42,43] have suggested a possible influence of age, sex, patient motivations/attitude or treatment expectations on outcome of wrist fracture, but such evidence on the prognostic value of these factors does not necessarily mean they can also predict a differential effect of treatment. Furthermore, methodological limitations in the conduct and reporting of results from available studies has limited the strength of evidence for effect moderation. All the potential moderators of treatment effect identified in this review are yet to be examined across large, adequately powered, randomised controlled trials. Most of the studies proposing potential moderators of treatment response did not formally investigate moderation, including testing of interaction or adequately presenting subgroup effects. As yet, evidence for moderators of treatment effect following wrist fracture is therefore lacking.

Implications for future research and practice

Based on currently available evidence, effectiveness of current rehabilitation protocols after wrist fracture is limited; and evidence for effect moderators is lacking as currently available trials are not large enough to produce data on sub-group effects with sufficient precision. To aid clinical practice and optimise effects of rehabilitation after wrist fracture, potential moderators need to be investigated in large trials or meta-analysis using individual participant data. Furthermore, the heterogenous nature of fractures and treatments as reported in current literature makes it difficult to draw conclusions about optimal timing of mobilisation. The reporting of rehabilitative interventions could be improved, including key features such as duration, dose or intensity, mode of delivery, and monitoring using for example prescriptions in the TIDIER checklist[44]. This will not only ensure adequate, homogeneous reporting essential for impactful evidence synthesis but will also aid research design and practice where rehabilitative needs of patients after wrist fracture are closely matched with elements and processes essential to the intervention.

Strengths and limitations

We have conducted a detailed systematic review of evidence using a comprehensive search of multiple databases, as well as considering grey literature. Although we considered articles that had been translated into the English language,[29] we excluded three articles that may have met our inclusion criteria due to lack of available translations (Fig.1). We used robust systematic review methods in line with established guidance including two independent reviewers for risk of bias and data extraction. Unfortunately, we were unable to conduct a meta-analysis due to insufficient data from studies both comparing the same interventions and using similar outcome measures. We acknowledge a generally low methodological quality among included studies. For instance, we found inconsistencies in reporting of the design, conduct and results of many of the included trials, which may have affected study results. Limitations included differences in baseline characteristics, treatment of control and intervention arms, and low sample sizes.

Conclusion

Evidence for the effectiveness of most rehabilitative treatments for reducing pain and improving function following wrist fracture is less than optimal. Moderation of the effects of exercise or occupational interventions on functional outcomes after wrist fracture by age (>55 years), sex (being female), or patient attitude/expectations of treatment could not be confirmed. However, there is very little evidence based on formal, high quality moderation analysis for these factors and there will be a need for these to be properly investigated in future pragmatic trials. This will be a first important step to more closely match the rehabilitative needs of patients with wrist fracture.

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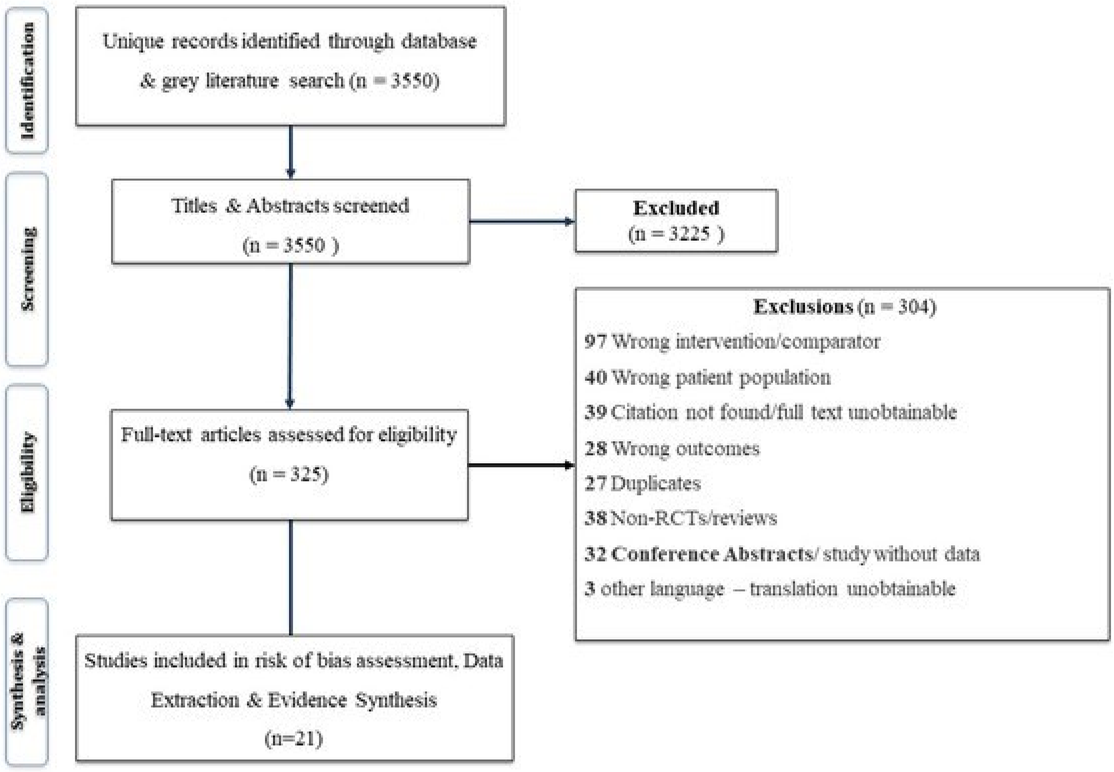

Figure 1: Study Flow chart

	Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome assessors	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias
Wollstein (2019)	?	×	?	×	✓	×	✓
Zlatkovi-Svenda (2019)	?	?	×	?	✓	✓	✓
Nguyen (2020)	✓	✓	✓	✓	✓	✓	✓
Tomruck (2020)	✓	✓	×	✓	✓	✓	✓
Clemensten (2019)	✓	✓	?	?	✓	✓	✓
Christensen (2001)	?	✓	?	?	?	×	?
Filipova (2015)	✓	×	×	✓	?	✓	✓
Gutierrez-Espinosa (2017)	✓	✓	?	✓	✓	✓	✓
Hakestad (2015)	✓	✓	?	✓	✓	×	✓
Jarus (2000)	?	?	?	?	?	×	✓
Kuo (2013)	✓	✓	?	?	✓	✓	✓
Magnus (2013)	✓	✓	✓	✓	✓	✓	✓
Miller-Shahabar (2018)	✓	✓	×	×	✓	✓	✓
Ratajczak (2015)	×	×	?	?	?	✓	?
Toomey (1986)	?	?	?	✓	✓	✓	×
Wakefield (2000)	✓	?	?	✓	✓	×	✓
Watt (2000)	?	?	?	✓	?	×	×
Maciel (2005)	✓	✓	?	✓	✓	✓	×
Bruder (2016)	✓	✓	?	✓	✓	✓	?
Dennison (2020)	✓	?	×	×	✓	?	✓
Dilek (2018)	✓	✓	?	?	✓	✓	✓

✓ **Low risk** ? **Unclear risk** × **High risk**

Figure 2: Risk of bias

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Table 1: Characteristics of included studies

First author	Country	Aim	Setting	N Randomised	N Lost to Follow Up	Diagnosis/ Fracture type & initial management	Eligibility	Mean Age *(SD/Range)*	Proportion Male (%)	Intervention			Control			Duration of follow-up (weeks)	Relevant Outcome Measures	Summary of Key Findings
										Description	Number of sessions	Duration of treatment (weeks)	Description	N of sessions	Duration of treatment (weeks)			
Bruder (2016)	Australia	Use of supervised exercise programme versus standard non-tailored physiotherapy	Community	33	4	DRF All initially managed by CR	>21y, and proficient language skills	54 (17.5)	24	Seven home exercises performed three times a day, which were assessed by physiotherapists during three physiotherapy sessions. Patients were then provided tailored advice.	3	3	Three standard PT consultations but no supervised advice or home exercise programme.	3	3	24	PRWE, wrist range of movement, grip strength and pain.	No clinically important or significant differences reported
Christensen (2001)	Denmark	Compare wrist function following OT verses HEP	Community	30	Not reported	Colles' Fracture Initially managed by CR "where necessary"	Colles' fracture	66 (46-82)	10	OT with functional, strength, and oedema focus along with control regime	Not stated	Not stated	HEP exercises to perform 3 times a week.	Not stated	Not stated	34.15	Werley Functional Score	No significant difference between the two groups.
Clemenstem (2019)	Norway	Early versus late mobilisation.	Community	119	7	DRF All initially managed by ORIF - VLP	18 to 70y with type A DRF with dorsal tilt, dorsal comminution, volar displacement or shortening >3mm	55(12)	66	Early mobilisation	6.5	13.05	Late mobilisation	1	13.05	104	Grip strength, pain, function	Only significant difference was in pronation being better in early mobilisation group at 6 weeks and 3 months but not at 1 year or 2 years. No significant difference in grip strength/ VAS/ QuickDASH/ PRWE. Early mobilisation and multiple formalised physiotherapy visits did not improve wrist function at any given time in the follow-up period (6 weeks, 3 months, 1 year, and 2 years postoperatively) compared with standard treatment of 2 weeks in a dorsal plaster splint, a single physiotherapy visit, and home exercises.
Dennison (2020)	USA	Early versus late motion following volar plating of DRF	Community	39	6	DRF/ulnar styloid All initially managed by ORIF - VLP	No previous DRF or significant comorbidities, and no extension of fracture in diaphysis or ulnar head, and surgical treatment with volar plating.	54 (16.5)	12.1	Home exercises started within 14 days of volar plating surgery.	130	52	Home exercises started 5 weeks after volar plating surgery.	130	52	52	DASH, PRWE and VAS	No significant difference between groups after 12 weeks.
Dilek (2017)	Turkey	GMI versus HEP.	Community	40	4	DRFs Included in randomisation: All initially managed by CR or ORIF - VLP	18-65y. Note: Excluded intra-articular or unstable DRFx,	49.9(10.15)	33.3.	Graded Motor Imagery (GMI) + Home Exercise Programme (HME) + structured physiotherapy	16	8	HEP + structured physiotherapy	16	8	8	PRWE, DASH, ROM and MHQ	Significant post-treatment improvement in the intervention group compared to the control group in pain at rest and during activity, flexion, extension, radial deviation and ulnar deviation. No difference in supination, pronation, grip strength or patient reported outcomes (MHQ score) between the two groups.
Filipova (2015)	Slovenia	Efficacy of combined physical and occupational therapy versus standard PT and advice.	Occupational healthcare	61	4	DRF All initially managed by CR	≥30y and stable conservatively managed DRF.	60 (14)	23	OT strengthening programme along with control intervention	9	3	PT ROM exercise, strengthening, & baths	9	3	13	ROM, grip strength, DASH	Intervention group had greater improvement in grip strength 12-16 weeks post-fracture compared to the control group. No significant difference in DASH or ROM reported.

Gutierrez-Espinosa (2017)	Chile	Supervised versus non-supervised PT.	Community	74	0	DRF All initially managed by CR	A3 extra-articular DRF with conservative management	71.9 (7.6)	4	Supervised PT with all patients receiving the same regime	12	6	Printed HEP and initial 30-min PT consultation proposed by Krischak et al	Not stated	5	6	PRWE, Grip strength, DASH, pain (VAS), ROM	Significantly higher treatment effect in intervention group for total PRWE, function, VAS, wrist extension and flexion and grip strength at 6 weeks and 6 months, but no significant difference between the groups for pain.
Hakestad (2015)	Norway	Effect of exercises with weight vests and a patient education programme versus standard advice brochure.	Community	80	16	Wrist fracture Specific type of fracture not stated Initial fracture management not stated but all were healed at inclusion.	Postmenopausal women ≥50y diagnosed with osteopenia, i.e., low BMD (t-score<=1.5), wrist fracture not older than 2 years and healed at inclusion	64.7 (7.1)	0	6-month home & group exercise balance, weight vests, coordination, core stability (OsteoActive) along with control intervention	78.3	26.1	Advice brochure with information on osteoporosis, risk factors, falls, and general exercise (OsteoInfo)	Not stated	Not stated	52	Quadriceps strength, BMD, physical capacity, SF-36	No significant results reported between control and intervention group at one year follow-up.
Jarus (2000)	Israel	Use of computer-aided brush machine versus standard OT brush machine.	Occupational healthcare	47	Not reported	Wrist Fractures: (35%, DRF, 53% Colles' fractures, 12% ulna or carpal bones or mixed fractures. All initially managed by CR or ORIF - VLP	Unilateral post-traumatic wrist fractures.	59.47(12.97)	19	OT brush machine with computer game modifications	15	5	Modified brush machine commonly used in OT departments	15	5	5	ROM, grip strength, oedema, interest,	No significant difference between the two groups.
Kuo (2013)	Taiwan	Early versus late mobilisation following external fixation.	Community	22	0	DRF All initially managed by ORIF - VLP	≥51y and external fixation surgery.	62.1 (6.1)	33	Early digit mobilisation until external fixator removal	18	6	Standard Advice regarding swelling control, fracture site protection, wound care, basic exercises at home	Not stated	7	12	MAM-36, grasp strength, dexterity, hand strength	Significantly increased digit movement in early mobilisation group at 12 weeks compared to control group.
Maciel (2005)	Australia	HEP versus focussed PT.	Outpatient	41	8	DRF All initially managed by CR	≥18y, cast removal, English language	55.75 (18.75)	24.39	HEP + activity focussed	Variable based on clinical judgment	6	HEP + single physiotherapy session	Not stated	6	24	PRWE score, grip strength, wrist extension and wrist flexion	No significant improvement in any outcome for the physiotherapy group vs exclusive home exercise group.
Magnus (2013)	Canada	Effect on outcomes of fractured wrist following cross-training of the unaffected arm.	Community	51	8	DRF All initially managed by CR	Women ≥50y	63 (10.1)	12	Cross training of non-fractured arm	78	26	HEP started after cast removal	42*	6	26	Grip strength, ROM, PRWE	Significant improvement in grip strength for intervention group compared to control group No significant difference in ROM or PRWE.
Miller-Shahabar (2018)	Israel	Use of compression glove versus standard PT.	Occupational healthcare	35	3	DRF All initially managed by CR (29%) or ORIF – VLP (71%)	≥18y, DRF, completed immobilisation & ≥2 hand symptoms	64.77 (11.29)	9	Compression glove 10h/d during rehab period along with control regime	42 (daily for 7 weeks)	6	Standard physiotherapy rehab	12	6	10.35	Oedema, PRWE, ROM, grip strength, self-reported Glove	Significant reduction in pain and functional disability in the intervention group compared to the control group at 4 weeks post-therapy. Significant increase in dynamic ROM at all time points for the intervention group compared to the control

																	questionnaire	group. No post-intervention statistical difference in static ROM, oedema or grip strength between the two groups.
Nguyen (2020)	Australia	Comparison of hand-strength exercises versus ROM exercises in conservatively managed DRFs in older patients.	Community	52	4	DRF All initially managed by CR	≥60 and conservatively managed	unclear	unclear	Hand strength focused exercise programme	4	4	Patient information sheet with general finger range of motion (ROM) exercises	4	12	12	Grip strength, QuickDASH, VAS pain score, radiographic parameters, adverse events	Significant improvement in QuickDASH, pain and grip strength at 12 weeks seen in the intervention group compared to the control group. No long-term follow-up.
Ratajczak (2015)	Poland	The effect of isometric massage on global grip strength after conservative treatment	Occupational healthcare	40	Not reported	DRF All initially managed by CR	DRF treated conservatively within 1 week of cast removal	43 (25-60)	45	Isometric massage along with control regime	10	2	Physio, laser therapy, magnetic field therapy, cryotherapy	14	2	2	Grip Strength	Significant increase reported in grip strength in both intervention and control but no significant difference between the groups. Subgroup analysis results: No differences as both women and men, younger and older patients had better global grip strength after rehabilitation combined with massage.
Tomruck (2020)	Turkey	Effects of early manual therapy on functional outcomes after volar plating.	Community	39	7	DRF All initially managed by ORIF- VLP	≥18y and proficient language skills who were treated with surgical treatment consisting of ORIF with a volar locking plate and screws.	51.5 (12.84)	46.7	Early manual therapy	24	12	Standard physiotherapy	24	12	12	PRWE, VAS and ROM, hand grip, hand strength and level of disability	Wrist flexion at 12 weeks was the only outcome that was significantly greater in the intervention group compared to the control group. No long-term follow-up.
Toomey (1986)	Canada	Clinical effects of whirlpool therapy versus hot towel.	Occupational Healthcare	24	Not reported	Colles' Fracture All initially managed by CR/ORIF	No associated fractures or complications, musculoskeletal conditions	59.665 *(6.395)*	16.67	Whirlpool therapy	12 (at participant's discretion)	maximum 6 (at participant's discretion)	Hot towel	12 (at participant's discretion)	maximum 6 (at participant's discretion)	not specified	ROM, pain, oedema, strength	No significant difference between groups.
Wakefield (2000)	Scotland	PT versus HEP	Outpatient	96	6	DRF "treated by variable periods of immobilisation in plaster"	≥55y, conservative management	73 *(9.45)*	9.4	Referred for a course of PT at their local health clinic or hospital along with control regime	Variable - at PT discretion	26	HEP	3 times a week	Variable (until patients were happy with the function of their hand).	26	Pain, ROM, Grip strength, functional assessment	Significant improvement in ROM (flexion and extension assessments) reported for PT-led group. Pain, grip strength and hand function did not significantly differ between the two groups.
Watt (2000)	Australia	PT versus HEP.	Outpatient	18	Not reported	Colles' Fracture Initial management not specified	No significant comorbidities	75.85 *(7.65)*	6	Supervised PT	5	6	HEP pamphlet	Not stated	Not stated	6	Wrist extension, Grip strength	Study reports significant improvement in grip strength and wrist extension in PT group compared to HEP.
Wollstein (2019)	USA	Pain and functional outcomes following sensorimotor rehabilitation versus standard physiotherapy	Community	60	Not reported	DRF All initially managed by ORIF- VLP	Adult patients treated with volar plating	63.9 (17)	17	Sensorimotor home rehab protocol	182	13	Physiotherapy	13	13	13.05	PRWE, proprioception and sensorimotor function	Significant improvement in sensorimotor testing for the intervention versus control group, but data are not portrayed.

Zlatkovi-Svenda (2019)	Serbia	Use of light therapy to prevent post-wrist fracture complications.	Community	55	3	DRF Initial management not specified	Females with wrist fracture	63 (7.05)	7	Bioptron (polarised, polychromatic, noncoherent, low-energy radiation) light	15	2	Anti-inflammatory drugs, exercises, and cryotherapy on the wrist and dorsal side of the hand	15	2	26.1	Pain and range of motion	Significant improvement in pain, and supination at day 15 for the intervention group compared to control, but these outcomes are not reported at 6 months. Reduced occurrence of CRPS at 6 months in intervention group, compared to control but may not be clinically significant-short term, small trial.

DRF: Distal radial fracture, **CR: closed reduction and cast immobilization, ORIF: open reduction and internal fixation, VLP: volar locking plate fixation,** PT: Physiotherapy, HEP: Home exercise programme, GMI: Graded motor imagery, PRWE: Patient-Rated Wrist Evaluation, DASH: Disabilities of the Arm, Shoulder, and Hand Questionnaire, ROM: range of motion, MHQ: Michigan Hand Outcomes Questionnaire.

Table 2 Summary of results for studies reporting pain and function outcomes of conservative treatments post wrist fracture.

All exercise interventions (PT/OT)							
First author, year of publication	**Intervention Category**	**Control Category**	**Length of follow-up**	**Summary results for pain**	**Results details + statistics**	**Summary results for function**	**Results details + statistics**
Bruder (2016)	HEP	PT/OT led exercise	24 weeks	Within arms, across all patients (reduced pain, positive effects) Between groups (minimal clinical difference. Non-statistically significant)	PRWE pain score Week 0 HEP: (mean PRWE pain score): 23, (SD 7) PT/OT: (mean PRWE pain score): 19, (SD 9) Week 7 HEP: (mean PRWE pain score): 10, (SD 5) PT/OT: (mean PRWE pain score): 10, (SD 11) Mean difference: –4 units, 95% CI –10 to 2 Week 24 HEP: (mean PRWE score): 7, (SD 7) PT/OT: (mean PRWE score): 5, (SD 6) Mean difference 0 units, 95% CI –3 to 3.	Improved function across patients No difference between groups	Weeks 0 HEP: (mean PRWE score): 23, (SD 9) PT/OT: (mean PRWE score): 25, (SD 11) HEP: (mean QuickDASH score): 39, (SD 14) PT/OT: (mean QuickDASH score): 44, (SD 24) Week 7 HEP: (mean PRWE score): 3, (SD 2) PT/OT: (mean PRWE score): 7, (SD 11) HEP: (mean QuickDASH score): 11, (SD 9) PT/OT: (mean QuickDASH score): 16, (SD 22) Mean difference: –5 units, 95% CI –16 to 6 Week 24 HEP: (mean PRWE score): 3, (SD 6) PT/OT: (mean PRWE score): 2, (SD 4) HEP: (mean QuickDASH score): 7, (SD 10) PT/OT: (mean QuickDASH score): 6, (SD 11) Mean difference: 0.3 units, 95% CI –6 to 7
Christensen (2001)	PT/OT	HEP	Not stated	-	-	Gradual improvement over time up till 9months for most patients but not significant difference No significant difference between groups.	Median Werley score 5 weeks PT/OT: 13 HEP: 12 P>0.05 3 months PT/OT: 8 HEP: 6 P>0.05 9 months PT/OT: 2 HEP: 3 P>0.05 No measure of variance.
Clemensten (2019)	Early mobilisation	Late mobilisation	104 weeks	Across all patients (no significant improvement at any given time points up to 2 years) Across groups (no difference between arms)	Mean VAS score Baseline Early: 0.1, SD (0.4) Late: 0.1, SD (0.4) 6 weeks Early: 1.8, SD (1.8) Late: 2.2, SD (1.7) Mean Difference (95% CI): 0.09 (−0.38; 0.56) P= 0.71 3 months Early: 1.1, SD (1.6) Late: 1.0, SD (1.2) Mean Difference (95% CI): 0.09 (−0.38; 0.55); P= 0.71 1 year Early: 0.7, SD (1.8) Late: 0.7, SD (1.2)	Across all patients (no significant improvement at any given time points up to 2 years) Across groups (no difference between arms)	Mean PRWE score Baseline Early: 0.7, SD (4.1) Late: 0.6, SD (2.4) 6 weeks Early: 29.6, SD (21.3) Late: 35.7, SD (21.2) P=0.14 3 months Early: 17.0, SD (18.6) Late: 15.9, SD (15.8) P=0.24 1 year Early: 10.2, SD (19.1) Late: 10.7, SD (15.4) P=0.24 2 years Early: 8.2, SD (17.2) Late: 8.0SD (14.9) P=0.72 **Mean QuickDASH score**

					Mean Difference (95% CI): 0.08 (−0.40; 0.56); P= 0.75 2 years Early: 0.7, SD (1.9) Late: 0.7, SD (1.5) Mean Difference (95% CI): 0.06 (−0.55; 0.68); P= 0.84		Baseline: Early: 2.2, SD (4.9) Late: 2.3, SD (5.6) 6 weeks Early: 29.5, SD (19.4) Late: 37.3, SD (19.1) P= 0.05 3 months Early: 17.1, SD (16.8) Late: 17.3, SD (14.4) P=0.06 1 year Early: 10.1, SD (17.9) Late: 10.7, SD (14.5) P= 0.20 2 years Early: 7.4, SD (14.5) Late: 7.4, SD (14.5) P= 0.53
Dennison 2020	HEP (early mobilisation)	HEP (late mobilisation)	1 year (2, 6, 8, 10, 12, 26, 52 weeks)	Across all patients (beneficial) Between groups (better for early mobilisation group at 6 weeks measured by VAS. No significant difference at any other follow-up points.	1 year follow-up Early: VAS (mean scores): 0.1 Late: VAS (mean score): 0.0 6 weeks follow-up Early: VAS (mean scores):0.8 Late: VAS (mean score):1.5 2 weeks follow-up Early: VAS (mean scores): 2.1 Late: VAS (mean score): 1.9 NB: results available for other follow-up points: 8, 10, 12, 26 weeks	Across all patients (beneficial) Between groups (better for early mobilisation group at 6 weeks measured by PRWE & DASH. No significant difference at any other follow-up points.	1 year follow-up Early: (mean scores) PRWE 5.4; DASH 6.0 Late: (mean scores): PRWE 5.1; DASH 5.3 6 weeks follow-up Early: (mean scores) PRWE 30; DASH 38 Late: (mean scores) PRWE 50; DASH 52 2 weeks follow-up Early: (mean scores) PRWE 55; DASH 59 Late: (mean scores) PRWE 66; DASH 73 NB: no mean difference or measure of deviation given
Filip ova (2015)	OT strengthening programme	PT/OT	13 weeks	Outcome non-specific to pain	-	Increased improvement across time point in combined PT/OT strengthening programme compared to PT alone for grip strength but not for DASH.	Mean DASH score (95% CI): Week 0 OT strengthening programme: 67 (61-73) PT/OT:68 (60–76) After intervention (week 3) OT strengthening programme: 39 (33–46) PT/OT:35 (29–41) Week 7-8 (one month after completing intervention) OT strengthening programme: 26 (21–32) PT/OT: 21 (15–26) T2:T1, T3:T1 DASH p<0.001 Group effect size: 0.023, p value: 0.264
Gutierrez-Espinosa (2017)	PT/OT led exercise	HEP	6 weeks	Across all patients (beneficial) Across all groups (beneficial)	Effect of treatment mean PRWE pain score 6 weeks PT PRWE pain score minus HEP PRWE pain score: 5.6 SD 8.1 CI (2.1 to 10.9) P= 0.039 6 months PT PRWE pain score minus HEP PRWE pain score: 2.5 SD 4.1 CI (-1.2 to 6.3) P=0.35 Effect of treatment mean VAS score 6 weeks	Across all patients (beneficial) Across all groups (beneficial) Improvement in pain and function from baseline to 6 weeks and 6 months in the treatment arm compared to the control group.	PRWE function 6 weeks PT PRWE function score minus HEP PRWE function score:15.2 (SD 10.6) CI (21.5 to 12.6) P<0.001 6 months PT PRWE function score minus HEP PRWE function score:14.5 (SD 12) CI (20.9 to 11.4) P<0.001

					PT PRWE pain score minus HEP PRWE pain score: 1.78 SD= 2.13 CI (2.43 to 1.13) P<0.001 6 months PT PRWE pain score minus HEP PRWE pain score: 0.97 SD= 1.38 SD 1.41 to 0.53) P<0.001		
Hakestad (2015)	PT/OT led exercise	HEP	1 year	Across all patients (nil beneficial effect for treatment/control arms) Between groups (no beneficial effect, no difference between groups).	Mean bodily pain measured using SF-36: Baseline PT/OT: 70.0, SD (23.1) HEP: 77.4, SD (22.3) 6 months PT/OT: 76.0, SD (25.0) HEP: 77.6, SD (26.1) Mean difference: −1.6 (−13.2, 9.9) One year PT/OT: 74.9, SD (22.5) HEP: 78.0, SD (27.7) Mean difference: −3.1 (−15.2, 8.9), p= 0.545	Across all patients (slightly worsened outcomes over follow up) Across groups (no significant differences between the two arms up to 1-year follow-up).	Mean SF-36 function score Baseline: PT/OT: 82.3, SD (16.7) HEP: 90.0, SD (11.7) 6 months PT/OT: 84.1, SD (18.7) HEP: 86.8, SD (20.0) Mean difference: −2.7 (−10.2, 4.8) 1 year PT/OT: 84.5, SD (14.1) HEP: 87.7, SD (12.0) Mean difference: −3.2 (−11.1, 4.6), p= 0.130
Kuo (2013)	Early digit mobilisation until external fixator removal (HEP)	Standard advice regarding swelling control, fracture site protection, wound care, basic exercises at home (HEP)	12 weeks	-	-	Some improvements in functional activity for patients in both groups. There were no significant differences between the groups throughout the follow-up period	MAM-36 score first assessment: 1 week after surgical fixation: Early: standard: 118:115, p=0.79 second assessment: 3 weeks after surgical fixation: Early: standard: 140:130, p=0.43 third assessment: 1 week after removal of the fixator; Early: standard: 156:144, p=0.22 fourth assessment: 12 weeks after surgical fixation Early: standard: 169:161, p=0.20
Maciel (2005)	PT/OT led exercise	HEP	24 weeks	Across patients within group: improvement over time at both 6 and 24 weeks (significant) Across patients between groups (similar improvement, no significant difference)	PRWE pain score Baseline PT/OT: 54.2, SD (21.1) HEP: 58.1, SD (19.5) 6 weeks PT/OT: 29.2, SD (23.4) HEP: 28.4, SD (19.2) 24 weeks PT/OT: 26.3, SD (25.4) HEP: 28.9, SD (21.3)	Patients in both arms improved with time but between groups, there was no significant difference in function after the intervention at 6 weeks or at follow-up at 24 weeks.	PRWE activity score Baseline PT/OT: 63.3, SD (28.9) HEP: 64.5, SD (25.0) 6 weeks PT/OT: 27.9 (28.2) HEP: 34.7, SD (28.2) 24 weeks PT/OT: 19.6, SD (29.4) HEP: 24.7, SD (26.4) Interaction effects reported as not significant. NB: no mean difference or actual effects data given.
Magnus (2013)	Cross-training + HEP	HEP	26 weeks	Not specific to pain- general PRWE score	-	Some improvements in function as assessed by PRWE for patients post treatment. However, there were no significant differences in PRWE scores between the training and control groups. at any time point up to 26 weeks.	Mean PRWE score Week 1 Cross training: 3.1, SD (4.2) HEP: 6.4, SD (6.0) Week 9 Cross training: 54.2, SD (39.0) HEP: 65.2, SD (28.9) Week 12 Cross training: 36.4, SD (37.2) HEP: 46.2, SD (35.3) Week 26 Cross training: 23.6, SD (25.6) HEP: 19.4, SD (16.5) "There are no significant differences."

							P values/ CI intervals not provided.
Nguyen (2020)	PT/OT Hand strength focused exercise programme	HEP	12 weeks	Across all patients (beneficial) Improvement in pain from week 2 to week 12. Between groups (beneficial) PT/OT was significantly beneficial at week 2 and week 12.	Mean/ median VAS Pain score (SD) <u>week 2</u> PT/OT: 3 (0-6) HEP: 5 (0-10) P= 0.0061 <u>Week 6</u> PT/OT: 3 (0-7) HEP: 3 (0-10) P= 0.57 <u>Week 12</u> PT/OT: 2.0 (0-5) HEP: 0 (0-4) P=0.046	Across all patients (beneficial) Between groups (beneficial) Significantly improved function from week 2 to week 12 but no significant difference between 2 to 6 weeks for between 6 and 12 weeks.	<u>Mean/ median QuickDASH score (SD)</u> <u>Week 2</u> PT/OT: 72.7 (29.5-88.6) HEP: 77.3 (29.5-93.2) P=0.15 <u>Week 6</u> PT/OT: 42.0 (6.8-72.7) HEP: 48.9 (4.5-86.3) P=0.19 <u>Week 12</u> PT/OT: 25.4 (20.9) HEP: 39.9 (21.9) 95% CI -1.01 to 29.93; P= 0.066
Ratajczak (2015)	Isometric massage + Combined PT led exercise, laser,magnetic field and cryo-therapy	PT led exercise, laser therapy, magnetic field therapy, cryotherapy	2 weeks	-	-	Global grip strength (proxy for function) increased significantly for both groups after intervention. No significant difference between groups.	<u>Grip strength</u> Mean grip strength (kg) pre-intervention: post-intervention for isometric massage vs standard care (SD): 12.85 (SD 8.31) :11.6 (SD 5.83) P=0.31
Tomruck (2019)	Early manual therapy (EMT)	PT/OT	12 weeks	All patients (beneficial). Between groups, the EMTG had significantly better PRWE total score, pain on VAS, wrist extension, ulnar/radial deviation, supination and grip strength at all time points, and better DASH score and wrist flexion at 12 weeks (P < 0.05).	Pain on VAS mean (SD) 3 weeks EMT: 2.8 (1.9) PT/OT: 5.5 (2.3) P=0.007 6 weeks EMT: 1.08 (1.24) PT/OT: 4.3 (2.5) P=0.001 12 weeks EMT: 0.58 (1.24) PT/OT: 3.3 (2.5) P=0.002 PRWE pain score 6 weeks EMT: 12.08 (6.20) PT/OT: 6.58 (5.73) PRWE pain score mean difference between groups: -5.50, SD (7.66); P=0.4	All patients (beneficial). Between groups difference reported, better performance for patients in EMT group	<u>Mean PRWE function score (SD)</u> 6 weeks EMT= 10.71 (6.50) PT/OT= 18.39 (13.75) P= 0.122 12 weeks EMT= 2.54, (3.49) PT/OT= 7.89, (4.98) P=0.005 Overall PRWE score change EMT= 8.17, (6.11) PT/OT= 10.50, (11.14) P=0.699 Overall DASH score change EMT= 15.84, (10.12) PT/OT= 19.78, SD (21.49) =0.918
Wakefield (2000)	HEP	PT/OT led exercise	26 weeks	For all patients in both treatment arms, pain reduced over time. Between groups (no significant difference in pain symptoms) Mean pain score difference (95% CI) <u>6 weeks</u> 0.3 (-0.5 to 1.2) <u>3 months</u> 0 (-0.7 to 0.7) <u>6 months</u> 0.1 (-0.7 to 0.8)	Mean difference in VAS <u>6 weeks</u> HEP: 2.3, SD (2.2) PT/OT: 2..0, SD (2.1) <u>3 months</u> HEP: 1.4, SD (1.6) PT/OT: 1.4, SD (1.7) <u>6 months</u> HEP: 0.9, SD (1.6) PT/OT: 0.8, SD (1.4)	Improved function within treatment arms up to 24 weeks. No difference between groups at any point or at end of follow up at 6months Mean difference HEP minus PT/OT (95% CI) <u>3 months</u> 0.7 (-3.4 to 4.7) P value 0.766 <u>6 months</u> 0.3 (-4.0 to 4.6) P value 0.437	<u>Mean difference in functional score:</u> <u>3 months</u> HEP: 88.3, SD (1.4) PT/OT: 87.6, SD (1.5) <u>6 months</u> HEP: 94.5, SD (1.5) PT/OT: 94.2, SD (1.5) P values/ CI intervals not provided.

Watt (2000)	HEP	PT/OT led exercise	6 weeks	-	-	Across all patients (beneficial) Across all groups (beneficial) Results questionable as error bars overlap	0 weeks HEP Grip strength: 1.0(0.3-1.4) PET Grip strength :1.3(0.1-2.6) 6 weeks HEP Grip strength: 5.3(4.3-6.1) PET Grip strength:10.0(7.0-13.5) P=0.026 NB: Data is median (interquartile range)
Wollstein (2019)	HEP	PT	13 weeks	Pain not formally assessed.	-	Functional improvement in both groups. Significant only for treatment arm at 3months.	Mean DASH score (SD) Baseline HEP= 72.9 (19.9) PT= 61.4 (22.7) 0=0.06 3 months HEP=33.7 (22.0) PT= 21.3 (17.4) P= 0.00.
Acupuncture, Electrotherapy etc (all non-exercise interventions (+other OT)							
First author, year of publication	**Intervention Category**	**Control Category**	**Length of follow-up**	**Summary results for pain**	**Results details + statistics**	**Summary results for function**	**Results details + statistics**
Zlatkovi-Svenda (2019)	Bioptron (polarised, polychromatic, noncoherent, low-energy radiation) light	Anti-inflammatory drugs, exercises, and cryotherapy on the wrist and dorsal side of the hand	26 weeks	Across all patients (positive) Between groups (positive) Mean pain significantly lower in light therapy group at day 15. "At the 6-month follow-up, CRPS occurrence was significantly reduced in the light therapy-treated group compared with the control group.	Mean VAS (SD) Day 0 Cryotherapy and exercise= 37.7 (1.7) Cryotherapy, exercise and light therapy= 33.1 (1.6) P=0.251 Day 7 Cryotherapy and exercise= 19.2 (1.2) Cryotherapy, exercise and light therapy= 16.2 (0.9) P=0.281 Day 15 Cryotherapy and exercise= 7.5 (9.8) Cryotherapy, exercise and light therapy= 2.1 (2.6) P=0.046 Day 7/ day 15 change 0.000 for both groups, p<0.01	-	No formal assessment of function.
Dilek (2017)	Graded Motor Imagery (GMI) + HEP+PT NB: Active intervention being tested is GMI	HEP+PT	8 weeks	Beneficial for all patients as mean pain within groups significantly reduced post intervention (may be due to multi-modal intervention - HEP +PT) GMI group were found to have significant reduction in pain as measured by VAS at rest and during activity compared to control group who had PT and HEP alone.	8 weeks follow-up: mean difference pre-post intervention (SD) GMI intervention: VAS @ rest 2.24 (2.08); VAS @ activity 6.18 (1.43) Control: VAS @ rest 1.11 (1.24); VAS @ activity 2.11 (0.81) P value (VAS @ rest): 0.005 P value (VAS @ activity): 0.001	Improved function for all patients post-intervention, as assessed by DASH & MHQ scores More benefit for patients in the GMI intervention group)	8 weeks follow-up: mean difference pre-post intervention (SD) GMI intervention: DASH 38.00 (14.33); MHQ -32.53(11.09) Control: DASH 26.58 (16.82); MHQ -19.68(10.40) P value (DASH): 0.048 P value (MHQ): 0.038
Jarus (2000)	OT computer-regulated brush machine	Modified brush machine commonly used in OT departments	5 weeks	Pain not assessed as an outcome	-	Across all patients significant improvement in grip strength and ROM. Between groups significant improvement in grip strength at	Functional outcome not assessed formally- grip strength as substitute. Grip strength (Kg) mean (SD) Baseline Brush= 21.29 (12.78)

						each time point better for computer aided.	Computer= 22.43 (7.66) Week 5 Brush=13.71 (12.32) Computer=11.39 (8.42) Overall difference computer- brush ANOVA approximated F Grip strength 71.17 p<0.01
Miller-Shahabar (2018)	Compression glove	Standard PT	4.5 weeks	Across all patients (beneficial) Across all groups (beneficial) Significant improvement in pain for both groups and significantly better in treatment group across all time points except at baseline (day 7-10).	PRWE mean pain scores (SD) <u>Day 7-10</u> Compression glove= 30.88 (9.46) PT= 36.27 (6.25) <u>Day 21-24</u> Compression glove=23.65 (9.46) PT= 34.80 (8.99) <u>One-month post-intervention (6weeks duration of intervention)</u> <u>Day 21-24</u> Compression glove= 19.82 (10.48) PT= 31.73 (9.79) <u>Effect of time compression glove group vs PT:</u> 14.98; p<0.001	Compared with the comparison group, the intervention. group showed a significantly greater reduction in functional difficulties but there were no significant within or between group differences for return to work.	<u>Functional difficulty in specific activities mean (SD)</u> <u>Day 7-10</u> Glove= 50.0 (10.85) PT= 56.13 (4.42) <u>Day 21-24</u> Glove= 33.24 (13.51) PT= 48.07 (6.42) <u>One-month post-intervention (6-week duration of intervention)</u> Glove= 24 (14.74) PT= 37.53 (11.03) Group effect: F(df=1,30) 11.46, p<0.01
Toomey (1986)	Whirlpool	Hot towel	Not specified	No significant changes.	Mean Present Pain Intensity (SD) <u>0 weeks</u> Whirlpool= 1.5 (1.31) Hot towel=1.42 (0.79) P=0.85 <u>6 weeks</u> Whirlpool= 0.75 (1.06) Hot towel=1.42 (1.31) P=0.18 <u>Follow up- not specified when</u> Whirlpool=0.42 (0.52) Hot towel=0.67 (0.89) P=0.41	Grip strength used as proxy for function. No significant changes.	Mean grip strength (SD) <u>0 weeks</u> Whirlpool= 2.5 (3.71) Hot towel= 1.83 (3.1) P=0.64 <u>6 weeks</u> Whirlpool= 1.42 (2.5) Hot towel= 1.75 (2.63) P=0.75 <u>Follow-up time not specified</u> Whirlpool=6.0 (5.51) Hot towel= 7.33 (5.4) P=0.56

- Pain not assessed as an outcome

Table 3a. Methodological Assessment of Moderation Analysis (Pincus et al. 2011)

Study	*A priori hypothesis*	Theory and/or Evidence driven hypothesis	Moderators measured prior to randomisation	Valid and reliable baseline and process factors	Explicit test of interaction	Total Score	Level of Moderation Evidence
Jarus (2000)	Yes	Yes	Unclear	Unclear	Yes	3	Exploratory
Ratajczak (2015)	No	Unclear	Yes	Yes	No	2	Insufficient
Levels of Moderation Evidence: Confirmatory Evidence: All 5 items met. Exploratory Evidence: 3+ items met; Insufficient Evidence: Failure to meet 3 items							

Table 3b: Summary of Moderators of treatment outcomes following wrist fracture.

Author (Year)	*Interventions studied*	*Prognostic factors explored or tested as potential moderators*	*Statistical analysis suggestive of moderation of treatment effect*	*Evidence for suggested moderator(s)/ Findings of moderation analysis on relevant outcome*	*Additional moderators (suggested) + Comments*	*Level of Moderation evidence (from Table 3a2)*
Jarus (2000)	Use of computer-aided brush machine versus standard OT brush machine.	Patient attitude towards computers	For each outcome measure (including grip strength as a proxy for function), a three-way analysis of variance (ANOVA) with repeated measures was performed: 2 (treatment group) x 2 (attitude) x 6 (time) design. Post hoc tests were then performed to test for significant differences. between the means. The level of significance was set at .05.	For function as measured by grip strength: the computer aided group improved more in grip strength than the control arm starting with the third time point; however, these differences were not significant at any time point. An enhanced interest in the computer-supported intervention was hypothesised to increase the motivation to repeat and continue to exercise and improve hand function. However, the interaction between treatment group and attitude toward computers on outcome was not significant.	Older age was suggested in the discussion section as a potential moderator of the effect of using a computer-aided brush machine compared to a standard machine, but this could not be investigated as most participants were older.	Exploratory
Ratajczak (2015)	Isometric massage + rehab package (combined PT-led exercises, cryotherapy, laser- and magnetic field- therapy) versus rehab package without massage	Age, sex	The change in global grip strength was presented for male and female patients, and for two age groups, separately within each treatment arm. No between-group differences were presented within age or sex subgroups, and no interaction tests were performed.	The descriptive analysis shows younger patients had greater grip strength at baseline than older patients, but improvements with treatment were similar for both age groups in both treatment arms. Grip strength also improved similarly in men and women irrespective of treatment group.	No other candidate moderators were suggested.	Insufficient

Figure legends

Fig.1: Prisma Flow Chart

Fig.2: Risk of bias in individual studies

Appendix : Full Medline search strategy

ORDAR - Wrist fracture intervention studies

MEDLINE ran 27.06.18 (Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present)

# ▲	Searches	Results
1	exp Fractures, Bone/	169266
2	fracture$.ti,ab,kw.	229140
3	exp Wrist Joint/	9355
4	Wrist Injuries/	5929
5	Wrist/	8207
6	(radius/ or ulna/ or forearm/ or forearm injuries/) and distal.ti,ab,kw.	4776
7	exp Carpal Bones/	8365
8	(wrist or colles$1 or smith$).ti,ab,kw.	46282
9	(capitate or hamate or lunate or pisiform or trapezium or triqeutrum or trapezoid or scaphoid).ti,ab,kw.	9071
10	((radius or radial or ulna$ or forearm$) and distal).ti,ab,kw.	18162
11	1 and (or/3-10)	11861
12	(1 or 2) and (or/3-7)	8242
13	Colles' Fracture/	845
14	((wrist or colles$1 or smith$) adj5 fracture$).ti,ab,kw.	2798
15	((capitate or hamate or lunate or pisiform or trapezium or triqeutrum or trapezoid or scaphoid) adj5 fracture$).ti,ab,kw.	2324
16	Ulna Fractures/ and distal.ti,ab,kw.	627
17	radius fracture/ and distal.ti,ab,kw.	3961
18	(((radius or radial or ulna$ or forearm$) adj5 fracture$) and distal).ti,ab,kw.	5604
19	or/11-18	14748
20	randomized controlled trial.pt.	462867
21	controlled clinical trial.pt.	92461
22	randomi#ed.ab.	495994
23	placebo.ab.	189808
24	clinical trials as topic/	183938
25	randomly.ab.	292750
26	trial.ti.	183807
27	or/20-26	1188338
28	exp animals/ not humans/	4467410
29	27 not 28	1095677
30	19 and 29	982

Appendix: Other suggested moderators – NB: not supported by evidence in design and analysis

Bruder (2016)	Participant outcome expectations may affect adherence and improve outcomes Not hypothesised a priori or planned in analysis
Christensen (2001)	Age, sex, fracture type, dominance Poor result related to comminution and joint involvement. Occupational therapy may not be suitable for damage of soft tissue structures around the wrist joint. A priori hypothesis was not set or planned for in analysis. Suggested in discussion.
Dennison (2020)	Duration of immobilisation (onset of rehabilitation) Fracture Classification (intra-/extra-articular) Although the late motion group had delayed recovery, there were no long-term (up to 1 yr) significant differences in motion, strength, outcome, or pain scores. Hypothesis not set a priori, planned for in analysis but no results and noted in discussion
Filipova (2015)	Age, sex, dominance Depression Patient expectations and patient-perceived outcome A priori hypothesis was not set or planned for in analysis. Suggested in discussion
Gutierrez-Espinosa (2017)	Age, sex, Immobilization time, dominance, fracture characteristics (aged >65yrs with more needs/complications). **A (**Malalignment as a predictor of poor functional outcome) Elderly (>65y) patients with complications may benefit from professional clinical supervision. May be beneficial to categorise into low and high demand groups. Malalignment is not a predictor of poor functional outcome A priori hypothesis was not set or planned for in analysis. Suggested in discussion
Hakestad (2015)	Age, height, weight, BMI, body fat, age of menarche, age of menopause, time since menopause, bisphosphanate, calcium use, past history of fracture, time since fracture, family history of OP, smoking hx, alcohol, education Multiple fallers may benefit in dynamic balance with an active rehab programme Patient adherence is possibly a moderating factor in active rehab programme Not hypothesised a priori or planned in analysis
Kuo (2013)	Age, sex, fracture type, dominance External fixator may be deterrent to early mobilisation and internal locking plate may be preferable Not hypothesised a priori or planned in analysis
Magnus (2013)	Age, Sex, Height, Weight Age may be a moderating factor, but was not explored due to the small sample size Surgical intervention may be a moderating factor, but was not explored due to small sample size Adherence may be a moderating factor, but was the same level in both arms Not hypothesised a priori or planned in analysis
Zlatkovi-Svenda (2019)	(Daily home exercises, poor balance control at baseline was associated with a better improvement in outcomes). poor balance control at baseline Daily home exercises Suggested in analysis and discussion
Tomruck (2020)	(Lower age in treatment group could have contributed to increased functional improvement) Lower age Active joint mobilizations in early postoperative period. Technique: Performing active joint mobilization in a pain-free ROM Suggested in analysis and discussion