Efficacy of non-surgical interventions for anterior knee pain: systematic review and meta-analysis of randomised trials

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Abstract

Anterior knee pain is a chronic condition that presents frequently to sports medicine clinics, and can have a long-term impact on active participation. Conceivably, effective early management may prevent chronicity and facilitate physical activity. Although a variety of non-surgical interventions have been advocated, previous systematic reviews have consistently been unable to reach conclusions to support their use. Considering a decade has lapsed since publication of the most recent data in these reviews, it is timely to provide an updated synthesis of the literature to assist sports medicine practitioners make informed, evidence-based decisions. A systematic review and meta-analysis was conducted to evaluate the evidence for non-surgical interventions for anterior knee pain.

A comprehensive search strategy was used to search MEDLINE, EMBASE, CINAHL and Pre-CINAHL, PEDro, PubMed, Sportdiscus, Web of Science, Biosis Previews, and the full Cochrane Library, while reference lists of included papers and previous systematic reviews were hand searched. Studies were eligible for inclusion if they were randomised clinical trials that used a measure of pain to evaluate at least one non-surgical intervention over at least two weeks in participants with anterior knee pain. A modified version of the PEDro scale was used to rate methodological quality and risk of bias. Effect size calculation and meta-analyses were based on random effects models.

Of 48 suitable studies, 27 studies with low to moderate risk of bias were included. There was minimal opportunity for meta-analysis due to heterogeneity of interventions, comparators and follow up times. Meta-analysis of high quality clinical trials supports the use of a six-week multimodal physiotherapy program (standardised mean difference 1.08, 95% confidence interval 0.73, 1.43), but does not support the addition of electromyography biofeedback to an exercise program in the short-term (four weeks: -0.21, -0.64 to 0.21; eight to 12 weeks: -0.22, -0.65 to 0.20).

Individual study data showed beneficial effects for foot orthoses with and without multimodal physiotherapy (*versus* flat inserts), exercise (*versus* control), closed chain exercises (*versus* open chain exercises), patella taping in conjunction with exercise (*versus* exercise alone), and acupuncture (*versus* control).

Findings suggest that, in implementing evidence-based practice for the non-surgical management of anterior knee pain, sports medicine practitioners should prescribe local, proximal and distal components of multimodal physiotherapy in the first instance for suitable patients, then consider foot orthoses or acupuncture as required.

1. Background

Anterior knee pain (AKP), or patellofemoral pain syndrome, is a chronic musculoskeletal overuse condition presenting frequently to sports medicine and general practitioners.[1-8] It affects an individual's ability to perform routine daily activities such as stair ambulation, walking and running, and thus impacts on work-related activities and participation in physical activity. Findings from prospective studies in active populations [9-11] reflect the chronicity of AKP, with a randomised controlled trial (RCT) reporting no recovery in half of the no-treatment control group at 12 months.[11] Furthermore, it is plausible that AKP in adults may precede the development of osteoarthritis in later years.[12]

Despite its prevalence, chronicity and impact, AKP remains one of the most challenging musculoskeletal conditions managed by practitioners.[13] Since greater pain severity and longer symptom duration are predictive of poor prognosis,[14] early effective management may be the key to limiting the longer-term impact of the condition. Considering the multifactorial nature of patellofemoral pain [15, 16], the management approach should consider individual presentation and the contribution of local knee factors, as well as potential proximal (hip) and distal (foot) factors.

Surgical options for AKP appear to be inadequate.[17] This is highlighted by a RCT that revealed no additional improvement in AKP symptoms and function over nine months when arthroscopic procedures based on pragmatically-identified abnormalities (e.g. resection of inflamed/scarred/excessive medial plicae or synovium, abrasion of chondral lesions, discision of lateral capsule, repair of meniscal tears) was added to exercise therapy.[18] Consequently, there is widespread consensus that non-surgical interventions are the primary treatment of choice for AKP. However, in order to make informed decisions regarding optimal management, practitioners require up-to-date, high quality evidence. Systematic reviews have drawn limited conclusions regarding RCT evidence for non-surgical interventions for AKP.[19-26] From these, it appears that there is moderate evidence to support the short-term use of patellar taping for chronic knee pain,[19, 26] however meta-analyses conducted by one review collapsed findings for nonarthritic AKP and patellofemoral joint osteoarthritis.[26] Considering the recent increase in research output regarding AKP interventions, it is timely for an updated high-quality systematic review to assist practitioners make informed, evidence-based decisions when managing AKP.[27] Therefore, a systematic review and meta-analysis, where possible, was conducted to evaluate the evidence for the short- and long-term efficacy of non-surgical interventions for AKP.

2. Methodology

The study protocol was developed in consultation with guidelines provided by the PRISMA Statement.[28]

2.1. Literature search strategy

Using guidelines provided by the Cochrane Collaboration,[29] a comprehensive search strategy was devised for the following databases: MEDLINE, EMBASE, CINAHL and Pre-CINAHL, PEDro, PubMed, Sportdiscus, Web of Science, Biosis Previews, and the full Cochrane Library. The MEDLINE search strategy, which was adapted for other databases, is presented in Appendix 1. All publications listed up until 30 November 2009 were considered for inclusion, with no restrictions placed on year of publication. Only full text, English language articles were included. Published abstracts were followed up for full text publications of the study, but were not included as stand-alone papers. One investigator (NC) reviewed all titles returned by the database searches, and retrieved suitable abstracts. Where abstracts suggested that papers were potentially suitable, the full text versions were obtained and included in the review if found to fulfil the selection criteria. Reference lists of included papers and known published systematic reviews were hand searched to ensure the inclusion of all available published evidence.

2.2. Selection criteria

Studies were eligible for inclusion if they investigated participants who had an insidious onset of anterior or retropatellar knee pain aggravated by activities that load the patellofemoral joint (PFJ) (e.g. prolonged sitting or kneeling, squatting, jogging or running, hopping, jumping, or stair ascending/descending).[30, 31] Studies were required to have investigated one or more non-surgical interventions for AKP, compared to a control intervention, over a minimum period of one week. The design must have been a clinical trial that i) followed participants over at least two weeks (deemed to be a clinically meaningful time period); ii) utilised an outcome measure of pain; such as pain measured on an 11-point numeric rating scale (NRS) or 100 millimetre visual analogue scale (VAS); and iii) randomly assigned participants to intervention groups using methods defined by PEDro rating scale criterion 2 (Appendix 2).[32] Studies were excluded if they presented results reported in a previous publication or if their sole focus was chondromalacia patella verified by imaging or arthroscopy.

2.3. Assessment of methodological quality and risk of bias

The methodological quality of included studies was rated using a modified version of the PEDro rating scale [32] (Appendix 2). This scale has been used in previous systematic reviews with very high inter-rater agreement (κ 0.73 to 0.824).[33, 34] Two independent reviewers (NC, LB), one of who remained blind to authors, affiliations and the publishing journal (LB), rated each study on 14 specific criteria. Final study ratings for each reviewer were collated and examined for discrepancies. Any inter-rater disagreement was discussed in a consensus meeting, and unresolved items taken to an independent party (BV) for resolution. Once consensus was reached for all study ratings, overall quality scores were determined for each study by summing those criteria that had scored "yes", providing a score out of 14.

Risk of bias was assessed using specific criteria from the modified PEDro scale, selected based on the PRISMA Statement [28] and the Cochrane Collaboration.[35] These were: adequacy of randomisation (criterion two); allocation concealment (criterion three); between-group baseline comparability (criterion four); blinding of outcome assessors (criterion seven); adequate follow-up (more than 85%) (criterion eight); and intention to treat analysis (criterion nine). A lack of blinding of participants and therapists was not considered to be a source of bias for these studies, as it is often not plausible to blind those providing and receiving interventions such as physiotherapy and specific exercises, particularly when the efficacy of two different interventions is compared. The RCTs were classified as having a low risk of bias (score 5 or 6 out of the 6 criteria), moderate risk (3 or 4) or high risk (≤ 2); the latter were excluded from further analysis.

2.4. Data management and statistical analysis

Inter-rater reliability of the modified PEDro scores was evaluated using the kappa (κ) statistic, where a κ of 0.9 to 1 represented almost perfect to perfect agreement, 0.7 to 0.9 very high agreement, 0.5 to 0.7 high agreement, 0.3 to 0.5 moderate agreement, 0.1 to 0.3 small agreement, and 0 to 0.1 very small agreement.[36]

Standardised mean differences (SMD) with 95% confidence intervals were used to represent effect sizes for pain, and were calculated using a random effects model in Review Manager (Version 4.2).[37] For studies that reported outcome on multiple pain scales, participant reported worst pain intensity over the previous week or a similar scale (e.g. pain with activity) was used. Data were grouped by follow-up time (0 to 6 weeks, 7 to 12 weeks, 13 to 26 weeks, greater than 26 weeks), using the latest time point in each period. Where possible, mean change scores and standard deviations were extracted from papers to calculate SMDs. Alternatively, mean change scores were calculated by subtracting the follow-up score from the baseline score, and the standard deviation estimated by taking the average of the pre- and post-score standard deviations [38] or 95% confidence intervals. When insufficient data prevented calculation of change scores, raw follow-up scores were used when groups were not significantly different on baseline measures from a clinical perspective (greater than 15 millimetres on a 100 millimetre pain VAS [39, 40]). Authors were contacted by email for clarification or provision of additional data. Effect size magnitudes were interpreted as being nearly perfect (SMD ≥ 4), very large (2 to 4), large (1.2 to 2), moderate (0.6 to 1.2), small (0.2 to 0.6) and trivial (< 0.2),[36] with positive values favouring the intervention of interest. A null effect was represented by a SMD with a confidence interval that crossed (but were not bound by) zero. Data were pooled where studies investigated similar interventions, and had similar comparator interventions and timing of follow-up outcome measures.

Sensitivity analyses were conducted to confirm the exclusion of papers with a high risk of bias. Since studies with higher quality scores return findings of reduced efficacy of treatment,[41] Spearman's correlation coefficients were calculated to determine the strength of the relationship between risk of bias (low, moderate, high) and effect size (SMD), and between modified PEDro scale score and effect size. The strength of correlations was determined using the same classification as for the κ statistic.[36]

3. Results

3.1. Search strategy

The comprehensive search strategy identified 605 publications for evaluation beyond title (Figure 1). The full text of 188 articles was retrieved, with 48 of these meeting the inclusion criteria.

3.2. Methodological quality and risk of bias

The 48 studies scored widely on the modified PEDro scale, ranging from two to 13 out of 14 (mean score 6.58) (see supplementary file). Criteria satisfied by less than half of the included papers were allocation concealment (criterion three, 29%), blinding (criterion five, 8%; criterion six, 2%; criterion seven, 41%), intention to treat analysis (criterion nine, 22%), justification of sample size (criterion 12, 37%), and reporting of adverse or side effects (criterion 14, 18%).

Initial inter-rater agreement on the modified PEDro criteria was very high (619 out of 672 ratings; $\kappa = 0.842$). Consensus was reached on all items on initial discussion. Inter-rater reliability for individual criteria ranged from high ($\kappa = 0.529$) for criterion eleven to perfect ($\kappa = 1.000$) for criteria one and two.

Twenty-one studies were considered to have a high risk of bias and subsequently excluded from further analysis (see Appendix 3 for study characteristics). Sensitivity analyses revealed a significant moderate correlation between risk of bias and SMD (correlation coefficient 0.328, $p = 0.004$), and between modified PEDro score and SMD (0.456, $p < 0.000$), supporting the exclusion of high-risk studies.

3.3. Findings

The 27 remaining studies were grouped by their primary intervention of interest (multimodal physiotherapy, manual therapy, exercise, tape, foot orthoses, electrotherapy, acupuncture, pharmacotherapy). Follow-up was predominantly within three months; only six studies followed participants beyond this. Table I presents characteristics of included studies with effect sizes for pain, and study conclusions when effect sizes could not be calculated.

3.3.1. Multimodal physiotherapy

Evidence from meta-analysis supports the use of multimodal physiotherapy in the short-term. Pooled data from two studies that investigated identical multimodal physiotherapy programs [30, 31] showed a significant moderate effect for multimodal physiotherapy over a placebo intervention (flat inserts [31]; sham physiotherapy [30]) at six weeks (SMD 1.08, 95% CI 0.73, 1.43) (Figure 2).

Evidence from individual RCTs largely supports the use of multimodal physiotherapy for AKP. When compared to placebo, there were significant moderate effects for multimodal physiotherapy at 12 weeks (0.69, 0.23 to 1.14), and significant small effects at one year (0.44, 0.01 to 0.88).[31] When multimodal physiotherapy was compared to a no-treatment or education control, the inclusion of more multimodal components appeared to increase its efficacy. Findings of Syme et al [42] showed significant moderate effects favouring eight weeks of manual therapy, stretches, vasti retraining and PFJ taping over no-treatment control (0.63, 0.00 to 1.26), but no significant effects were seen when only manual therapy, stretches and general lower limb exercises were used. However, there were contrasting effects found by Clark et al, [43] who reported no significant effects when a combination of exercise, patellar taping and education was compared to education alone at 12 weeks and one year.

Effect sizes predominantly showed favourable effects for multimodal physiotherapy compared to other non-surgical interventions, although this appeared to be associated with timing of outcome measures. From the study of Collins et al [31] there were significant small effects favouring multimodal physiotherapy over foot orthoses at six weeks (0.51, 0.07 to 0.95) and 12 weeks (0.45, 0.01 to 0.88), but no significant differences at one year. Furthermore, the addition of multimodal physiotherapy to foot orthoses when compared to foot orthoses alone produced significant moderate effects at all time points over one year (six weeks: 0.87, 0.42 to 1.32; 12 weeks: 0.63, 0.16 to 1.07; 52 weeks: 0.70, 0.27 to 1.14). Harrison et al [44] compared multimodal physiotherapy (patella taping, vasti retraining) to a home exercise program (general lower limb strengthening and stretching) with and without therapist supervision over one year. There was a significant small effect favouring the multimodal program over supervised exercise at four weeks (0.56, 0.00 to 1.12). Interestingly, multimodal physiotherapy was not significantly different to supervised or unsupervised exercise at 12, 26 or 52 weeks.

When compared to placebo, multimodal physiotherapy used in conjunction with foot orthoses produced significant large effects at six weeks (1.45, 0.96 to 1.94), and significant moderate effects at 12 weeks (0.86, 0.40 to 1.33) and 52 weeks (0.77, 0.33 to 1.21).[31] However, the combined effects of multimodal physiotherapy and foot orthoses were not significant when compared to physiotherapy alone at six, 12 or 52 weeks (Figure 2).

3.3.2. Exercise

Evidence from individual RCTs supports the use of various forms of exercise for AKP (Figure 3). Three studies showed significant effects favouring exercise over a no-treatment control.[11, 45, 46] Herrington and Al-Sherhi [45] compared two different six-week programs of knee extension exercises (closed kinetic chain; open kinetic chain) to no-treatment control. Effect sizes calculated from data provided by the authors showed significant large to very large effects favouring both types of exercise over control (closed chain: 3.02, 1.93 to 4.11; open chain: 1.82, 0.95 to 2.69). Effect sizes for Song et al [46] showed significant moderate effects favouring leg press with hip adduction (0.83, 0.26 to 1.40) and standard leg press (1.01, 0.43 to 1.59) over control after eight weeks. Similarly, findings of van Linschoten et al [11] showed significant small effects for supervised exercise therapy over control at 12 weeks (0.44, 0.09 to 0.78) and at one year (0.49, 0.14 to 0.83).

Interestingly, time effects were found among studies that compared closed and open kinetic chain strengthening exercises. Contrasting effects were found for two short-term studies, with Herrington and Al-Sherhi [45] showing a significant moderate effect favouring closed chain over open chain exercises at six weeks (1.01, 0.25 to 1.78), while a similar study by Bakhtiary et al [47] showed no significant effects at five weeks. In comparison, a five-year follow-up study showed a significant small effect in favour of open chain exercises (-0.57, -1.14 to 0).[48]

Two studies evaluated hip exercises as an addition to standard exercise programs (Figure 3). Findings of Nakagawa et al [49] showed no significant effect on worst pain severity for the addition of hip abduction and external rotation exercises to standard quadriceps exercises. Similar outcomes were noted in the study of Song et al,[46] with effect sizes showing no significant effects when leg press was performed in hip adduction compared to the standard leg press exercise.

Comparison of two groups from the study of Harrison et al [44] investigated the effect of physical therapist supervision of a home exercise program (Figure 3). Effect sizes revealed no significant difference between supervised and unsupervised exercise at four, 12, 26 or 52 weeks.

Three studies investigated the use of exercise as an adjunct to other interventions (Figure 3). Effect sizes revealed no significant effect for the addition of exercise to education over 12 and 52 weeks,[43] to patellar mobilisation/manipulation over five weeks,[50] or to foot orthoses over four or eight weeks.[51]

3.3.3. Foot orthoses

Evidence from one RCT supports the short-term use of foot orthoses over placebo (Figure 4). Collins et al [31] showed a significant small effect for foot orthoses over flat inserts at six weeks (0.59, 0.15 to 1.04), but no differences in effect at 12 weeks or one year. One study compared foot orthoses to exercise.[51] While effect sizes showed no significant difference at four or eight weeks, sample size calculations provided by the authors indicated that the study was underpowered to detect significant effects.

Effect sizes calculated from four- and eight-week data provided by Wiener-Ogilvie and Jones [51] were not significant when foot orthoses were used in conjunction with exercise, compared to exercise alone (Figure 4), although post hoc power calculations conducted by the authors suggested a high likelihood of a type II error.

3.3.4. Patella taping

Evidence from one RCT supports the short-term use of patella taping (Figure 4). Effect sizes from Whittingham et al [52] showed significant large to very large effects favouring four weeks of patella taping and exercise over exercise alone (2.47, 1.25 to 3.70), and over placebo tape with exercise (1.35, 0.36 to 2.35). In contrast, longer-term data from Clark et al [43] showed no significant between-group effects when patella taping and education was compared to education alone, and when patella taping was added to exercise and education (12 and 52 weeks).

3.3.5. Acupuncture

Evidence provided by one RCT supports the use of acupuncture in AKP (Figure 4). Effect sizes calculated from data provided by Jensen et al [53] showed a significant moderate effect favouring acupuncture treatment over control at five month follow up (0.65, 0.13 to 1.16). Although outcome measures were also taken at two other time points over a year, only the acupuncture group was followed up at six weeks, and pain severity was not recorded at one year.

3.3.6. Manual therapy

All three studies that investigated manual therapy techniques compared to control or in conjunction with other interventions revealed no significant findings (Figure 4). Van den Dolder et al [54] showed no significant effect for two weeks of treatment with medial glide and tilt mobilisations and local lateral retinacular massage when compared to a no-intervention control. Similar outcomes were found for joint manipulation. Findings of Brantingham et al [55] showed no significant effect at six or 14 weeks for either knee manipulation or full lower limb kinetic chain manipulation when each was added to exercise and soft tissue treatment. In the study by Stakes et al [56], there was no significant effect for the addition of spinal manipulation to patellar mobilisation over four weeks.

3.3.7. Electrotherapy

Evidence from meta-analysis does not support the use of electromyography (EMG) biofeedback in addition to an exercise program (Figure 4). Pooled data from two studies [57, 58] showed no significant benefit of using EMG biofeedback with exercise at four weeks (-0.21, -0.64 to 0.21), or at eight to 12 weeks (-0.22, -0.65 to 0.20).

Electric muscle stimulation (EMS) was investigated by two studies (Figure 4).[59, 60] Effect sizes from Akarcali et al,[59] who evaluated the addition of high voltage pulsed galvanic stimulation to an exercise program, showed no significant effect for either group at six weeks. Callaghan et al [60] compared different EMS devices, finding no significant effects for either simultaneous mixed frequency or sequential mixed frequency EMS. One study compared low level laser treatment to sham laser over five weeks,[61] however insufficient data was provided for effect size calculation.

3.3.8. Pharmacotherapy

One study investigated pharmacological interventions for AKP,[62] comparing one week of NSAIDs to placebo; however the authors did not report data for effect size calculation.

4. Discussion

The comprehensive search strategy identified a wide variety of conservative interventions for AKP that have been investigated by RCTs. Meta-analyses of pain data, the primary symptom of this condition, provides evidence for multimodal physiotherapy when compared to a placebo over six weeks, as well as evidence of no additional benefit in adding EMG biofeedback to exercise over 12 weeks. Due to a lack of further opportunities for data pooling, the best evidence for other interventions such as exercise, patella taping, foot orthoses and acupuncture comes from individual RCTs.

Findings from this review indicate that multimodal physiotherapy, compared to a placebo intervention that controls for therapist-patient interaction effects, has the best evidence for reducing AKP using a non-surgical approach. Importantly, the magnitude represents a clinically meaningful improvement in pain, with the weighted mean difference of 20.3 millimetres out of 100 exceeding the minimal clinically important difference.[39, 40] The two studies incorporated in the meta-analysis received the highest ratings on the modified PEDro scale, scoring 13[30] and 12 [31] out of 14. Importantly, identical multimodal programs were used, and incorporated interventions targeting local factors (patellar taping, patellar mobilisation, vasti retraining with EMG biofeedback), proximal factors (gluteal strengthening) and global factors (lower limb stretches). Syme et al [42] also included these components in their multimodal program, which was more efficacious than no treatment. In contrast, the multimodal programs of Clark et al [43] and Harrison et al [44], who reported largely non-significant differences to comparators, only utilised local interventions and did not target proximal or distal factors. This suggests that the inclusion of interventions that target specific proximal factors,[63] as utilised by Crossley et al [30] and Collins et al [31], either in conjunction with local interventions or as stand-alone interventions, may be the key to ensuring success in reducing AKP symptoms. Importantly, these findings highlight the multifactorial nature of AKP,[64] and the need for practitioners to use clinical judgement to address all necessary lower limb factors to effectively manage this condition. However, more RCTs are required to facilitate further meta-analyses, particularly evaluating multimodal physiotherapy compared to a no-treatment control as well as the effects of proximal interventions used in isolation. Furthermore, considering that only one study investigated long-term outcomes of multimodal physiotherapy,[31] this should be considered in future studies.

Findings of the three studies that compared exercise to wait-and-see indicate that a predominantly quadriceps-based program is more effective than no treatment.[11, 45, 46] However, it appears that the addition of hip components, supervision, or other adjunct interventions to quadriceps-based programs does not change AKP outcomes. It is important to highlight that these studies tended to lack specific vasti retraining, instead aiming for general quadriceps strengthening. This may explain differences in effects of combined treatments when multimodal physiotherapy outcomes are compared to those of exercise studies. Furthermore, these findings highlight the importance of targeted exercise programs based on sound clinical assessment, with consideration of additional components and interventions as necessary. While it is difficult to draw conclusions regarding direct comparison of open and closed kinetic chain exercises, the greater emphasis on closed-chain exercises in the other exercise and multimodal programs suggests that this is the preferred clinical approach, and fits with evidence of greater vasti activity during closed than open kinetic chain exercises.[65]

It is important to note that the apparent lack of evidence for other interventions such as pharmacotherapy and manual therapy does not imply that these interventions are not effective; rather, it highlights deficits in the current literature with respect to study methodology as well as the need for more high-quality RCTs. Small sample sizes utilised by some of these studies may have increased the risk of a type II error. It is also important to consider those interventions that were not sufficiently represented in the 27 studies, such as knee braces and trunk muscle retraining. Indeed, six studies evaluated the efficacy of knee and patella braces,[66-71] but were excluded due to high risk of bias, while only one study incorporated transversus abdominus retraining into their exercise program [49]. Importantly, no studies were found that investigated interventions targeted to individual participant presentations, such as core stability deficits. Thus, these simple and commonly used interventions require further investigation utilising high-quality RCT design.

This is the first systematic review to incorporate meta-analyses of data from RCTs investigating conservative interventions solely for nonarthritic AKP. It also considers 23 RCTs of low to moderate risk of bias that were not included in the most recent published systematic review of all non-surgical interventions,[21] or have been published since. New evidence from pooled data was found regarding multimodal physiotherapy and EMG biofeedback. However, other non-surgical interventions including pharmacology require ongoing investigation. This is particularly important considering the role that early effective intervention, aimed at reducing pain severity and duration, may play in limiting the longer-term impact of AKP.[14]

Despite the strengths of this systematic review, there are limitations that need to be considered when interpreting findings. Studies were not considered eligible for inclusion if they were published in non-English languages. While it is arguable that authors of high-quality RCTs would aim to widely disseminate their findings via high-impact journals published in the English language, it is plausible that this may influence outcomes of analyses. Furthermore, while the use of a rigorous and systematic methodology limits the influence of potential biases, assessment of publication bias was not conducted. Considering that publication bias has been reported for studies investigating patellar taping and bracing for chronic knee pain [26], it is possible that publication bias also exists among studies of other interventions for AKP, and only highlights the need for further high-quality RCTs to ensure that the literature is characterised by more balanced findings.

A number of methodological issues were identified among the included studies that should be addressed in future AKP RCTs. Firstly, the 48 studies initially rated for their methodological quality had a mean modified PEDro rating of less than half of the total possible score, and almost half of these studies were excluded from further analysis due to a high risk of bias associated with the study design or inadequate reporting. In order to enhance the quality of published studies on AKP, and maximise the potential for consolidation of findings in systematic reviews and meta-analyses, future RCTs should utilise Consolidated Standards of Reporting Trials (CONSORT) guidelines [72] during the methodological design phase and when reporting study findings. This would also address the inconsistencies and inadequacies with reporting outcome data that were observed, and the subsequent effect that this has on calculation of effect sizes and meta-analyses. Secondly, participant numbers were generally low, with final group sizes below 30 for the majority of studies. Only 37 percent of the 48 studies reported sample size calculations, which suggests that they may not have been adequately powered to show significant between-group differences. Thirdly, only six studies included in final analyses investigated treatment effects beyond three months. In the context of a chronic condition such as AKP,[9] studies of longer duration are required to determine the longer-term efficacy of interventions.

While the aim of this systematic review was to investigate the effect of interventions on pain, future RCTs should consider using a range of outcome measures that also address other signs and symptoms of AKP. The Kujala Patellofemoral Score [73] which encompasses pain, function and other symptoms, has been shown to be reliable, valid and responsive in AKP,[40] and predictive of short- and long-term outcome.[14] Indeed, it was used as an additional outcome measure in 11 of the 48 studies initially included.[11, 14, 40, 45, 48, 55, 60, 66, 74-76] Ratings of global improvement [31] provide an overall opinion of treatment effects on the condition as a whole, and can be represented by clinically meaningful statistics such as relative risk reduction and numbers needed to treat. More widespread use of such measures would facilitate further between-study comparisons and meta-analyses involving dimensions other than pain.

5. Conclusion

Pooled data from a limited subset of studies supports the use of multimodal physiotherapy incorporating proximal as well as local interventions to reduce AKP in the short term, but does not support the addition of EMG biofeedback to exercise. Due to a lack of further opportunities for data pooling, individual RCTs provide the best evidence for other interventions such as exercise, patella taping, foot orthoses and acupuncture. Until further high-quality RCTs are conducted addressing issues of sample size, long-term follow up and adherence to the CONSORT statement, sports medicine practitioners should prescribe local, proximal and distal components of multimodal physiotherapy for appropriate AKP patients, but also consider foot orthoses or acupuncture as adjunct or alternative interventions.

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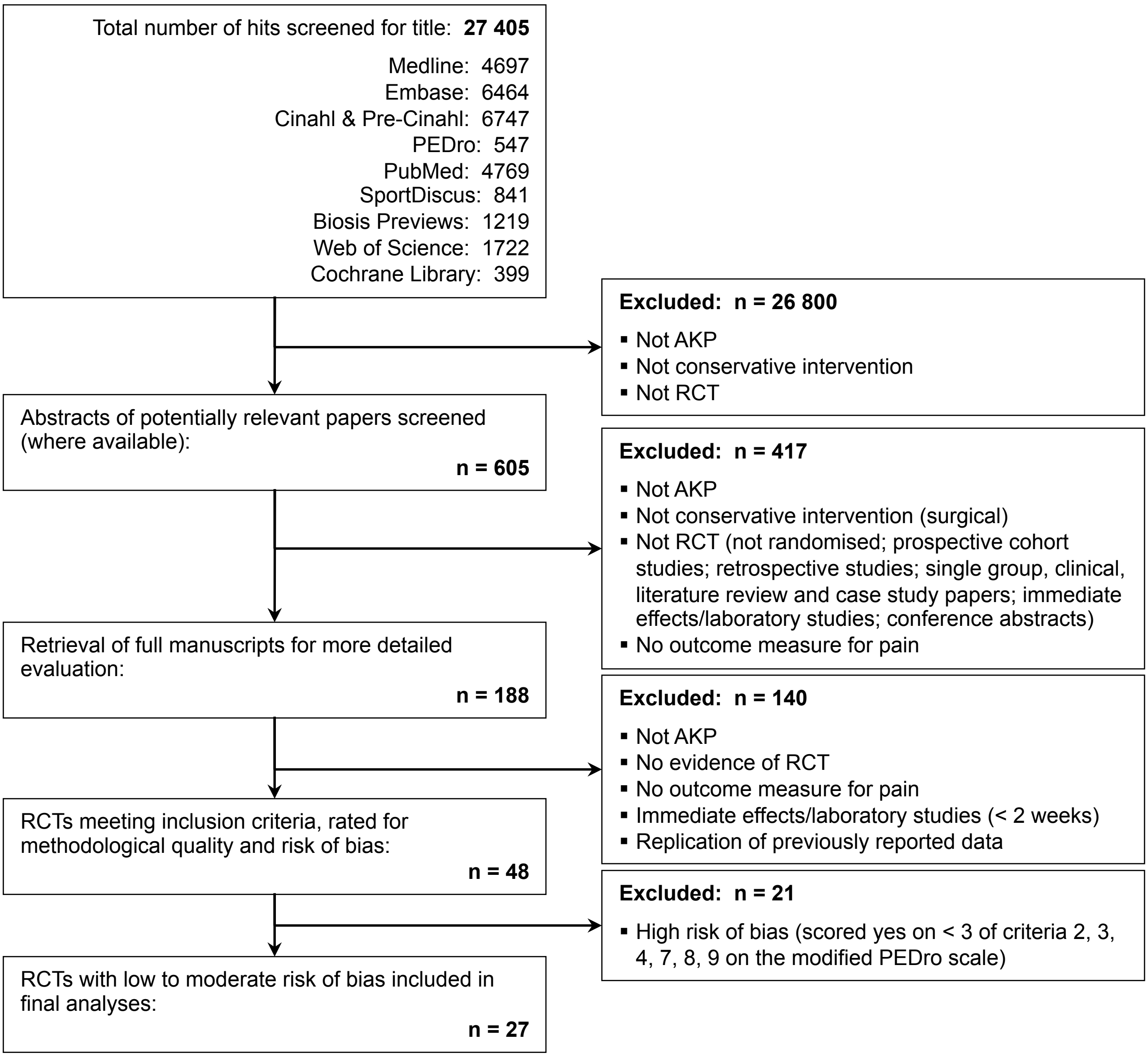
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▪ Not conservative intervention
▪ Not RCT
Abstracts of potentially relevant papers screened (where available):
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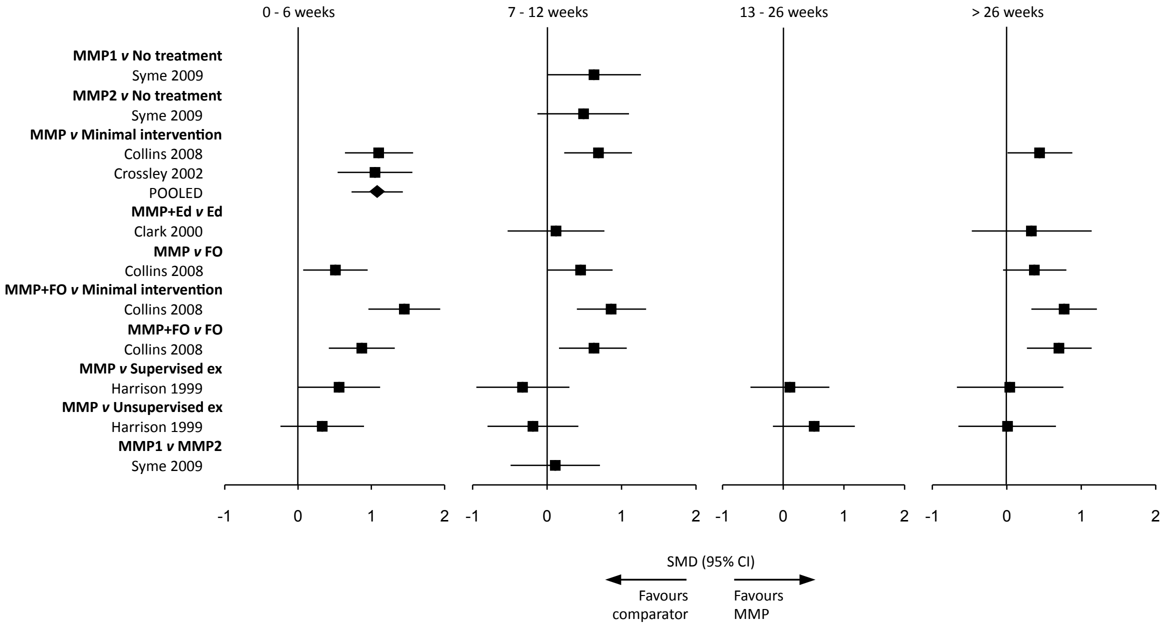
Excluded: n = 417
▪ Not AKP
▪ Not conservative intervention (surgical)
▪ Not RCT (not randomised; prospective cohort studies; retrospective studies; single group, clinical, literature review and case study papers; immediate effects/laboratory studies; conference abstracts)
▪ No outcome measure for pain
Retrieval of full manuscripts for more detailed evaluation:
n = 188
Excluded: n = 140
▪ Not AKP
▪ No evidence of RCT
▪ No outcome measure for pain
▪ Immediate effects/laboratory studies (< 2 weeks)
▪ Replication of previously reported data
RCTs meeting inclusion criteria, rated for methodological quality and risk of bias:
n = 48
Excluded: n = 21
▪ High risk of bias (scored yes on < 3 of criteria 2, 3, 4, 7, 8, 9 on the modified PEDro scale)
RCTs with low to moderate risk of bias included in final analyses:
n = 27


0 - 6 weeks
7 - 12 weeks
13 - 26 weeks
> 26 weeks
MMP1 v No treatment
Syme 2009
MMP2 v No treatment
Syme 2009
MMP v Minimal intervention
Collins 2008
Crossley 2002
POOLED
MMP+Ed v Ed
Clark 2000
MMP v FO
Collins 2008
MMP+FO v Minimal intervention
Collins 2008
MMP+FO v FO
Collins 2008
MMP v Supervised ex
Harrison 1999
MMP v Unsupervised ex
Harrison 1999
MMP1 v MMP2
Syme 2009
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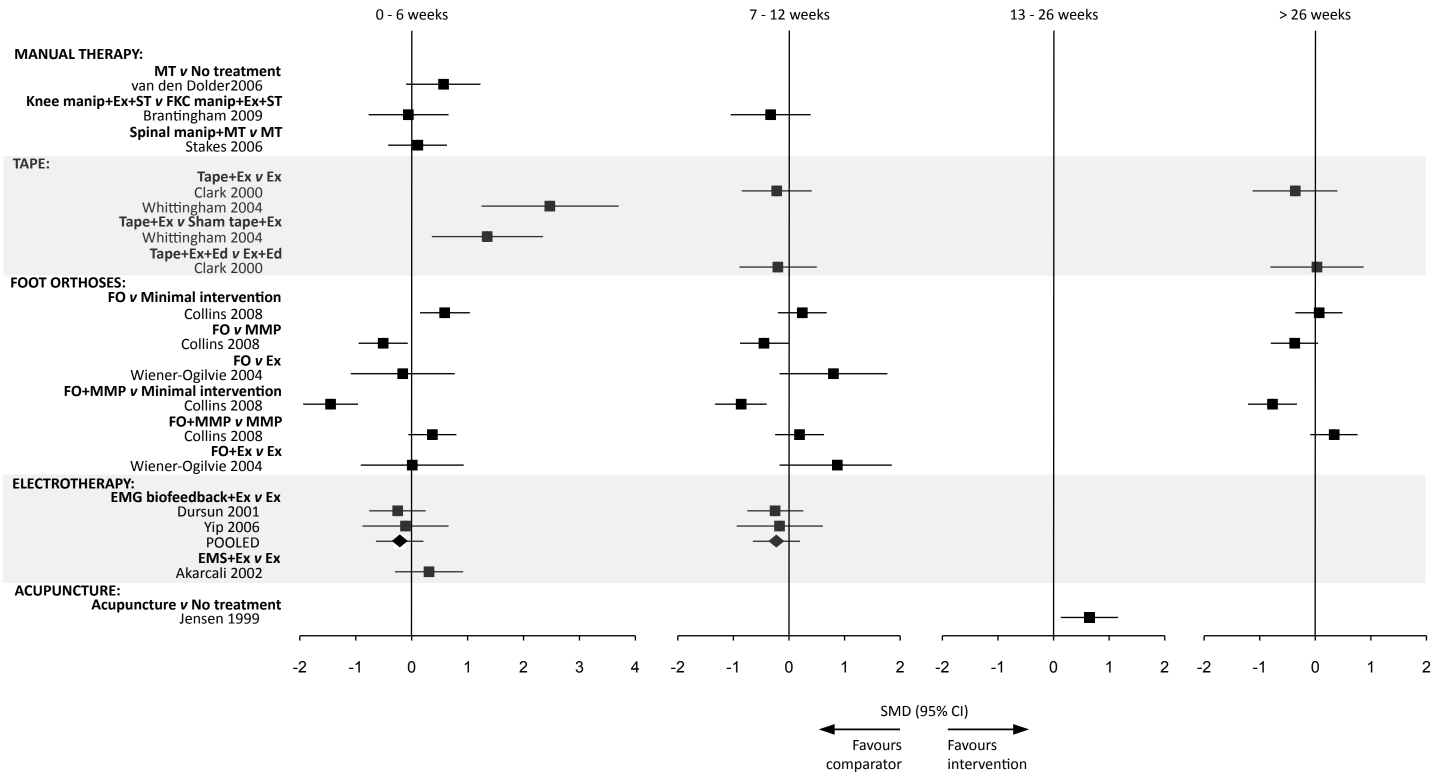
0
1
2
SMD (95% CI)
Favours comparator
Favours MMP


0 - 6 weeks
7 - 12 weeks
13 - 26 weeks
> 26 weeks
MANUAL THERAPY:
MT v No treatment
van den Dolder2006
Knee manip+Ex+ST v FKC manip+Ex+ST
Brantingham 2009
Spinal manip+MT v MT
Stakes 2006
TAPE:
Tape+Ex v Ex
Clark 2000
Whittingham 2004
Tape+Ex v Sham tape+Ex
Whittingham 2004
Tape+Ex+Ed v Ex+Ed
Clark 2000
FOOT ORTHOSES:
FO v Minimal intervention
Collins 2008
FO v MMP
Collins 2008
FO v Ex
Wiener-Ogilvie 2004
FO+MMP v Minimal intervention
Collins 2008
FO+MMP v MMP
Collins 2008
FO+Ex v Ex
Wiener-Ogilvie 2004
ELECTROTHERAPY:
EMG biofeedback+Ex v Ex
Dursun 2001
Yip 2006
POOLED
EMS+Ex v Ex
Akarcali 2002
ACUPUNCTURE:
Acupuncture v No treatment
Jensen 1999
-2 -1 0 1 2 3 4
-2 -1 0 1 2
-2 -1 0 1 2
-2 -1 0 1 2
SMD (95% CI)
Favours comparator
Favours intervention

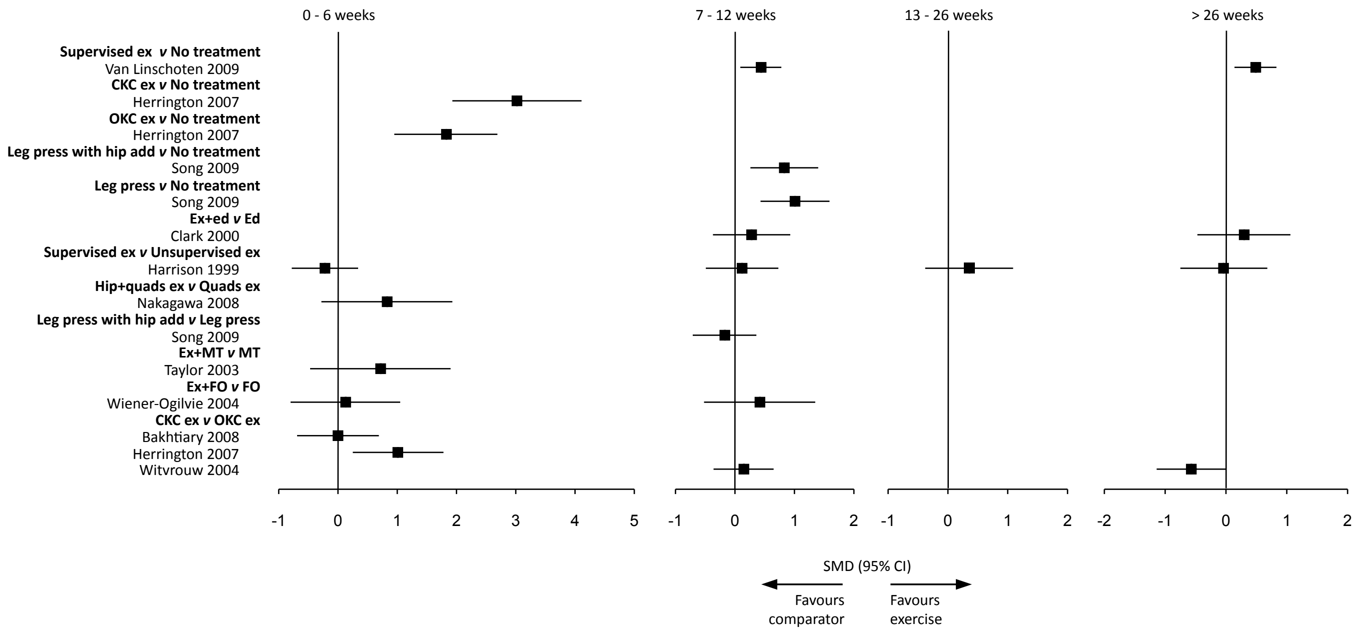

0 - 6 weeks
7 - 12 weeks
13 - 26 weeks
> 26 weeks
Supervised ex v No treatment
Van Linschoten 2009
CKC ex v No treatment
Herrington 2007
OKC ex v No treatment
Herrington 2007
Leg press with hip add v No treatment
Song 2009
Leg press v No treatment
Song 2009
Ex+ed v Ed
Clark 2000
Supervised ex v Unsupervised ex
Harrison 1999
Hip+quads ex v Quads ex
Nakagawa 2008
Leg press with hip add v Leg press
Song 2009
Ex+MT v MT
Taylor 2003
Ex+FO v FO
Wiener-Ogilvie 2004
CKC ex v OKC ex
Bakhtiary 2008
Herrington 2007
Witvrouw 2004
-1 0 1 2 3 4 5
-1 0 1 2
-1 0 1 2
-2 -1 0 1 2
SMD (95% CI)
Favours comparator
Favours exercise

Table I. Summary of included studies (N = 27).

	INTERVENTION:		SAMPLE:			EFFECT SIZE FOR PAIN AT FOLLOW-UP (weeks)		
Study (modified PEDro rating)		**Duration (weeks)**	**Total randomised (total analysed) per group**	**Mean (SD) age (years) #median**	**Mean (SD) knee pain duration (months) #median (IQR)**	**Comparison**	**SMD (95% CI)**	**Study conclusions (where effect size = ID)**
MULTIMODAL PHYSIOTHERAPY								
Clark 2000 [43] (9/14)	A: Exercise (quadriceps, gluteals) + patella taping + education D: Education	12	A: 20 (16,10) D: 22 (21,15)	A: 26 (7.4) B: 27.1 (7.2)	NR	A vs D	12: 0.12 (-0.53 to 0.77) 52: 0.33 (-0.47 to 1.14)	
Collins 2008 [31] (12/14)	A: Foot orthoses B: Flat inserts C: Physiotherapy (patella taping, vasti retraining with EMG biofeedback, gluteal strengthening, patella mobilisation, stretches) D: Foot orthoses + physiotherapy	52	A: 46 (41, 42, 45) B: 44 (40, 38, 41) C: 45 (41, 41, 42) D: 44 (42, 40, 43)	A: 27.9 (5.3) B: 29 (6) C: 30.9 (5.8) D: 29.6 (5.6)	A: 42 (12.3-96)# B: 24 (12-71)# C: 37 (12.3-84.8)# D: 24 (9-60)#	C vs B (worst) C vs A (worst) D vs B (worst) D vs A (worst)	**6: 1.10 (0.64 to 1.57)** **12: 0.69 (0.23 to 1.14)** **52: 0.44 (0.01 to 0.88)** **6: 0.51 (0.07 to 0.95)** **12: 0.45 (0.01 to 0.88)** 52: 0.37 (-0.05 to 0.80) **6: 1.45 (0.96 to 1.94)** **12: 0.86 (0.40 to 1.33)** **52: 0.77 (0.33 to 1.21)** **6: 0.87 (0.42 to 1.32)** **12: 0.63 (0.16 to 1.07)** **52: 0.70 (0.27 to 1.14)**	
Crossley 2002 [30] (13/14)	A: Physiotherapy (patella taping, vasti retraining with EMG biofeedback, gluteal strengthening, patella mobilisation, stretches) B: Sham physiotherapy	6	A: 36 (33) B: 35 (34)	A: 29 (8) B: 26 (8)	A: 39 (43) B: 31 (32)	A vs B (worst)	**6: 1.05 (0.54 to 1.56)**	
Harrison 1999 [44] (8/14)	A: Physiotherapy (patella taping, vasti and hip adductor exercises, EMG biofeedback) + education B: Home exercise program (quadriceps, hip adductors) monitored by physical therapist + education C: Home exercise program + education	4	A: 36 (25,20,23,18) B: 34 (26,20,15,13) C: 42 (23,22,14,18)	22.2 (8.2)	NR	A vs C (worst) A vs B (worst)	4: 0.33 (-0.24 to 0.90) 12: -0.19 (-0.80 to 0.42) 26: 0.51 (-0.17 to 1.18) 52: 0.01 (-0.65 to 0.66) **4: 0.56 (0.00 to 1.12)** 12: -0.33 (-0.95 to 0.30) 26: 0.11 (-0.54 to 0.76) 52: 0.04 (-0.67 to 0.76)	
Syme 2009 [42] (11/14)	A: Physiotherapy (patella mobilisations) with selective VMO retraining (EMG biofeedback, patella taping) B: Physiotherapy with general quadriceps strengthening	8	A: 23 (21) B: 23 (22) C: 23 (20)	A: 28.8 (8) B: 27.3 (7.9) C: 28.5 (6.4)	A: 49 (37.5) B: 45.5 (35.3) C: 50.5 (41.3)	A v B A v C B v C	8: 0.11 (-0.49 to 0.71) **8: 0.63 (0.00 to 1.26)** 8: 0.49 (-0.13 to 1.10)	

	INTERVENTION:		SAMPLE:			EFFECT SIZE FOR PAIN AT FOLLOW-UP (weeks)		
		Duration (weeks)	**Total randomised (total analysed) per group**	**Mean (SD) age (years) #median**	**Mean (SD) knee pain duration (months) #median (IQR)**	**Comparison**	**SMD (95% CI)**	**Study conclusions (where effect size = ID)**
EXERCISE								
Clark 2000 [43] (9/14)	B: Exercise (quadriceps, gluteals) + education D: Education	12	B: 20 (16,12) D: 22 (21,15)	B: 29.5 (6.2) D: 27.1 (7.2)	NR	B vs D	12: 0.28 (-0.37 to 0.93) 52: 0.30 (-0.47 to 1.06)	
Harrison 1999 [44] (8/14)	A: Home exercise program (quadriceps, hip adductors) + education B: Home exercise program monitored by physical therapist + education	4	A: 42 (23,22,14,18) B: 34 (26,20,15,13)	22.2 (8.2)	NR	B vs A	4: -0.22 (-0.78 to 0.34) 12: 0.12 (-0.49 to 0.73) 26: 0.36 (-0.38 to 1.09) 52: -0.04 (-0.75 to 0.68)	
Herrington 2007 [45] (8/14)	A: WB knee extension (leg press) B: NWB knee extension (sitting) C: No-treatment control	6	A: 15 (15) B: 15 (15) C: 15 (15)	26.9 (5.6)	NR	A vs C B vs C	**6: 3.02 (1.93 to 4.11)** **6: 1.83 (0.95 to 2.69)**	
Nakagawa 2008 [49] (8/14)	A: Hip + quadriceps exercises B: Quadriceps exercises	6	A: 7 (7) B: 7 (7)	23.6 (5.9)	NR	A vs B (worst)	6: 0.83 (-0.28 to 1.93)	
Song 2009 [46] (11/14)	A: Leg press with hip adduction B: Leg press C: No-treatment control	8	A: 29 (27) B: 30 (27) C: 30 (25)	A: 38.6 (10.8) B: 40.2 (9.9) C: 43.9 (9.8)	A: 41.8 (36.1) B: 38.3 (34.2) C: 27.7 (41)	A vs C A vs B B vs C	**8: 0.83 (0.26 to 1.40)** 8: -0.17 (-0.71 to 0.36) **8: 1.01 (0.43 to 1.59)**	
Taylor 2003 [50] (9/14)	A: Quadriceps exercises + patella mobilisation/manipulation B: Patella mobilisation/manipulation	4	A: 6 (6) B: 6 (6)	30.17 (NR)	NR	A vs B	5: 0.72 (-0.47 to 1.90)	
Van Linschoten 2009 [11] (9/14)	A: Supervised exercise therapy B: No-treatment control	52	A: 65 (65,65) B: 66 (66,66)	A: 24.7 (8.6) B: 23.3 (7.8)	NR	A vs B (activity)	**12: 0.44 (0.09 to 0.78)** **52: 0.49 (0.14 to 0.83)**	
Wiener-Ogilvie 2004 [51] (9/14)	A: Foot orthoses C: Exercise (quadriceps, hamstrings, hip adductors) + foot orthoses	8	A: 11 (9) C: 10 (9)	A: 38.7 (17.2) C: 61.8 (10.3)	A: 17.9 (17.8) C: 29.8 (38)	C vs A	4: 0.13 (-0.80 to 1.05) 8: 0.42 (-0.52 to 1.35)	
Closed vs. open chain exercises:								
Bakhtiary 2008 [47] (6/14)	A: Closed kinetic chain exercises (semi-squat) B: Open kinetic chain exercises (SLR)	3	A: 16 (NR) B: 16 (NR)	A: 21.8 (0.6) B: 22.3 (1.7)	NR	A vs B	5: 0.00 (-0.69 to 0.69)	
Herrington 2007 [45] (8/14)	A: WB knee extension (leg press) B: NWB knee extension (sitting)	6	A: 15 (15) B: 15 (15)	26.9 (5.6)	NR	A vs B	**6: 1.01 (0.25 to 1.78)**	
Witvrouw 2000 [76] (6/14)	A: Closed kinetic chain exercises B: Open kinetic chain exercises (quadriceps, hip adductors)	5	A: 30 (30) B: 30 (30)	20.3 (NR)	15.1 (NR)	A vs B	5: ID~ 12: ID~	Group A had significantly greater improvement in night pain (*p* = 0.024) & pain during testing (*p* = 0.028); no significant differences on 11 other pain VAS (*p* > 0.05).
Witvrouw 2003 [77] (9/14)	A: Closed kinetic chain exercises B: Open kinetic chain exercises (quadriceps, hip adductors)	5	A: 30 (30) B: 30 (30)	20.3 (NR)	15.1 (NR)	A vs B	5: ID~ 12: ID~	No significant difference at 5 & 12 weeks (*p*>0.05).
Witvrouw 2004 [48] (6/14)	A: Closed kinetic chain exercises B: Open kinetic chain exercises (quadriceps, hip adductors)	5	A: 30 (30) B: 30 (30)	20.3 (NR)	15.1 (NR)	A vs B	12: 0.15 (-0.36 to 0.65) **260: -0.57 (-1.14 to 0)**	

	INTERVENTION:		SAMPLE:			EFFECT SIZE FOR PAIN AT FOLLOW-UP (weeks)		
		Duration (weeks)	**Total randomised (total analysed) per group**	**Mean (SD) age (years) #median**	**Mean (SD) knee pain duration (months) #median (IQR)**	**Comparison**	**SMD (95% CI)**	**Study conclusions (where effect size = ID)**
TAPE								
Clark 2000 [43] (9/14)	A: Exercise (quadriceps, gluteals) + taping + education B: Exercise + education C: Taping + education D: Education	12	A: 20 (16,10) B: 20 (16,12) C: 19 (18,12) D: 22 (21,15)	A: 26 (7.4) B: 29.5 (6.2) C: 29.3 (6.8) D: 27.1 (7.2)	NR	C vs D A vs B	12: -0.22 (-0.85 to 0.41) 52: -0.36 (-1.13 to 0.40) 12: -0.20 (-0.89 to 0.50) 52: 0.03 (-0.81 to 0.87)	
Whittingham 2004 [52] (10/14)	A: Patella taping + exercise B: Placebo taping + exercise C: Exercise (quadriceps, hip external rotators)	4	A: 10(10) B: 10(10) C: 10 (10)	A: 18.8 (1.3) B: 18.6 (1.1) C: 18.7 (1.4)	NR	A vs C A vs B	**4: 2.47 (1.25 to 3.70)** **4: 1.35 (0.36 to 2.35)**	
FOOT ORTHOSES								
Collins 2008 [31] (12/14)	A: Foot orthoses B: Flat inserts C: Physiotherapy (patella taping, vasti retraining with EMG biofeedback, gluteal strengthening, patella mobilisation, stretches) D: Foot orthoses + physiotherapy	52	A: 46 (41, 42, 45) B: 44 (40, 38, 41) C: 45 (41, 41, 42) D: 44 (42, 40, 43)	A: 27.9 (5.3) B: 29 (6) C: 30.9 (5.8) D: 29.6 (5.6)	A: 42 (12.3-96)# B: 24 (12-71)# C: 37 (12.3-84.8)# D: 24 (9-60)#	A vs B (worst) A vs C (worst) D vs B (worst) D vs C (worst)	**6: 0.59 (0.15 to 1.04)** 12: 0.24 (-0.20 to 0.68) 52: 0.07 (-0.36 to 0.49) **6: -0.51 (-0.95 to -0.07)** **12: -0.45 (-0.88 to -0.01)** 52: -0.37 (-0.80 to 0.05) **6: 1.45 (0.96 to 1.94)** **12: 0.86 (0.40 to 1.33)** **52: 0.77 (0.33 to 1.21)** 6: 0.37 (-0.06 to 0.80) 12: 0.19 (-0.25 to 0.63) 52: 0.34 (-0.09 to 0.76)	
Wiener-Ogilvie 2004 [51] (9/14)	A: Foot orthoses B: Exercise (quadriceps, hamstrings, hip adductors) C: Foot orthoses + exercise	8	A: 11 (9) B: 10 (9) C: 10 (9)	A: 38.7 (17.2) B: 51 (22.5) C: 61.8 (10.3)	A: 17.9 (17.8) B: 10.6 (8.2) C: 29.8 (38)	A vs B C vs B	4: -0.16 (-1.09 to 0.77) 8: 0.80 (-0.17 to 1.77) 4: 0.01 (-0.91 to 0.93) 8: 0.87 (-0.17 to 1.85)	
MANUAL THERAPY								
Manual PFJ techniques:								
van den Dolder 2006 [54] (11/14)	A: PFJ mobilisation B: No-treatment control	2	A: 21 (21) B: 17 (16)	A: 55 (11) B: 52 (18)	A: 26 (12-91) B: 39 (15-137)	A vs B (average)	2: 0.57 (-0.10 to 1.23)	
Manipulation:								
Brantingham 2009 [55] (8/14)	A: Knee manipulation + exercises + soft tissue treatment B: Full kinetic chain manipulation + exercises + soft tissue treatment	6	A: 25 (13) B: 22 (18)	A: 27.9 (3.2) B: 30.7 (8.1)	A: 48.5 B: 54.8	A vs B (worst)	2-6: -0.06 (-0.77 to 0.66) 10-14: -0.33 (-1.05 to 0.39)	
Stakes 2006 [56] (6/14)	A: Spinal manipulation + patellar mobilisation B: Patellar mobilisation	4	A: 30 (28) B: 30 (28)	A: 29 (NR) B: 32 (NR)	NR	A vs B	4: 0.11 (-0.42 to 0.63)	

	INTERVENTION:		SAMPLE:			EFFECT SIZE FOR PAIN AT FOLLOW-UP (weeks)		
		Duration (weeks)	**Total randomised (total analysed) per group**	**Mean (SD) age (years) #median**	**Mean (SD) knee pain duration (months) #median (IQR)**	**Comparison**	**SMD (95% CI)**	**Study conclusions (where effect size = ID)**
ELECTROTHERAPY								
Rogvi-Hansen 1991 [61] (7/14)	A: Low level laser treatment B: Placebo (sham laser)	5	A: 20 (19) B: 20 (17)	A: 35 (NR) B: 31 (NR)	A: 48 (NR) B: 72 (NR)	A vs B	5: ID 8-12: ID	No statistical difference between groups (p>0.05).
EMG biofeedback:								
Dursun 2001 [57] (6/14)	A: Exercise (quadriceps, VMO) + EMG biofeedback B: Exercise	12	A: 30 (30) B: 30 (30)	A: 36.9 (9.2) B: 36.6 (10.6)	A: 10.8 (7.7) B: 9.7 (8.1)	A vs B	4: -0.25 (-0.76 to 0.25) 12: -0.25 (-0.75 to 0.26)	
Yip 2006 [58] (8/14)	A: Exercise (quadriceps, VMO) + EMG biofeedback B: Exercise	8	A: 13 (13) B: 13 (13)	32.5 (8.8)	NR	A vs B	4: -0.11 (-0.88 to 0.66) 8: -0.17 (-0.94 to 0.61)	
Electric muscle stimulation:								
Akarcali 2002 [59] (7/14)	A: High voltage pulsed galvanic stimulation + exercise (open progressing to closed kinetic chain) B: Exercise	6	A: 22 (20) B: 22 (22)	A: 41.6 (9.58) B: 36.3 (9.59)	15.74 (9.31)	A vs B	6: 0.31 (-0.30 to 0.92)	
Callaghan 2004 [60] (10/14)	A: Simultaneous 5-frequency EMS B: Single frequency EMS	6	A: 39 (37) B: 41 (37)	A: 36.5 (13.6) B: 33.2 (9.4)	A: 30.5 (15.25) B: 25.75 (15.5)	A vs B	6: ID~	No significant differences between groups in post-treatment pain (p = 0.249).
ACUPUNCTURE								
Jensen 1999 [53] (8/14)	A: Acupuncture B: No-treatment control	4	A: 37 (36,30,nr) B: 38 (34,31,nr)	A: 29 (NR) B: 33.4 (NR)	A: 76.8 (NR) B: 81.6 (NR)	A vs B	6: ID **20: 0.65 (0.13 to 1.16)** 52: ID	Did not test control group at 6 weeks or measure pain at 52 weeks.
Qiu 2009 [80] (5/14)	A: Warming needle + exercise (quadriceps, hip adductors) B: NSAID (Meloxicam) + exercise	4	A: 49 (47) B: 49 (45)	A: 54 (NR) B: 55 (NR)	A: 6 (NR) B: 12 (NR)	A vs B	1: ID 2: ID 3: ID 4: ID	No between-group comparisons for pain.
PHARMACOTHERAPY								
Suter 1998 [62] (6/14)	A: NSAID (Naproxen sodium) B: Placebo	1	A: 22 (19) B: 20 (17)	35.6 (8.4)	NR	A vs B	1: ID~	Group A had significantly greater reduction in pain than Group B in affected and unaffected knees (p < 0.05).

NR: not reported in article; ID: inadequate data provided by authors; ~ no significant difference between groups (p = 0.05); ID~ authors only reported statistical significance (between-group)
n/a: no outcome measure for pain; SMD in bold denotes significant effect; VMO: vastus medialis obliquus; SLR: straight leg raise; WB: weight bearing; NWB: non-weight bearing; ROM: range of motion; PNF: proprioceptive neuromuscular facilitation; ITB: iliotibial band; NSAIDs: nonsteroidal anti-inflammatory drugs; TENS: transcutaneous electric nerve stimulation; EMG: electromyography; EMS: electric muscle stimulation; NSAID: nonsteroidal anti-inflammatory drug.