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Effects of strength training, multimodal exercise and manual mobilization on pain and function in knee osteoarthritis: A systematic review and meta-analysis

Anna Frances Quillfeldt, Rebecca Melissa Marks

ABSTRACT

Osteoarthritis is a major contributor to pain and disability, and while ample evidence suggests that exercise and manual therapy are beneficial for improving pain and function of sufferers, the body of research lacks evidence comparing the different intervention types. A systematic review with meta-analysis was performed to determine the effect of strength training, multimodal exercise therapy and manual mobilization on pain and physical function in people with osteoarthritis of the knee. A search of MEDLINE, PEDro, and CINAHL was performed (January 2009 – May 2014). Trials incorporating either strength training alone, multi-modal exercise (strength training and active range of motion exercises with or without aerobic activity) or exercise plus additional manual mobilization were included. Meta-analyses were performed for each intervention type and both pain and physical function outcome measures. Results: Data from eight eligible studies was integrated. The search did not reveal trials comparing the effects of manual mobilization and exercise therefore this comparison could not be analyzed. Strength training demonstrated a larger effect size [pain = 1.26 (95% CI 0.97 to 1.55); physical function =1.15 (95% CI 0.87 to 1.44)] compared to multi-modal exercise [pain = 0.47 (95% CI 0.24 to 0.69); physical function = 0.53 (95% CI 0.30 to 0.75)]. In conclusion, Strength training and multi-modal exercise were both found to be effective in reducing pain and improving physical function in people with osteoarthritis of the knee. Strength training alone revealed more favorable effect sizes than multi-modal exercise.

Keywords: Arthritis, Exercise, Knee osteoarthritis, Manual therapy, Strength training

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INTRODUCTION

Osteoarthritis (OA) of the knee is the most common form of arthritis and has the potential to result in significant pain and disability [1]. With an ageing population and a rise in obesity rates, knee OA is becoming an increasing concern, therefore health professionals need to provide effective, inexpensive and accessible solutions to support sufferers and manage symptoms [1]. Exercise plays an essential role in the management of knee OA and the importance of therapeutic strength training, aerobic and range of motion exercises has been emphasized in current literature [2–4]. It has been suggested that the addition of manual mobilization provides increased benefits regarding pain and physical function when compared to strength training alone or to multi-modal exercise [4]. The purpose of this review is to compare the current literature analyzing the effects of strength training, other exercise interventions and manual mobilization for people with knee OA, with regard to changes in pain and physical function. To achieve this, a systematic review of the literature was carried out to provide an overview of current research, conduct a critical appraisal and a meta-analysis of the relevant studies. The authors' aim is to guide health care professionals towards optimizing patient care in order to improve outcomes and reduce disability in people with knee OA.

METHODS

Study selection and data collection

Using MEDLINE, PEDro and CINAHL, a systematic search was performed to identify eligible studies from January 2009 – May 2014. January 2009 was chosen in order to continue the search of a similar review [4] that incorporated available literature from January 1990 to December 2008. Keywords included in the search were 'knee', 'exercise', 'physical therapy modalities', 'musculoskeletal manipulations' and 'randomized controlled trial'. A group of eight reviewers assessed the studies for their relevance and quality. Studies were considered to be relevant if they were randomized controlled trials that included any exercise intervention or manual therapy intervention compared to a non-exercise control group. Included studies needed to measure the outcomes of pain and physical function of participants with knee OA, as these outcome measures were used in the meta-analysis. These outcome measures belong to the core set of outcomes for phase III trials in OA [5, 6]. Aquatic-based studies, studies not published in English and studies that do not measure the results immediately post-intervention were excluded (Figure 1). Any discrepancies were resolved by consensus or iteration. The studies were categorized into one of the following codes: Code 1 = strength training only; Code 2 = multimodal exercise therapy; Code 3 = exercise plus manual mobilization. Strength training was defined as any intervention using moderate or heavy strength training as defined in the studies. Multimodal exercise included strength training and active range of motion exercises with or without aerobic activity. Manual mobilization was defined as any passive physical or manual therapy to the affected lower limb. Inconsistencies in coding were resolved by consensus. The quality of the studies was assessed using criteria from the Evidence Based Richtlijn

Design
- Randomised controlled trials

Participants
- Adults with osteoarthritis of the knee, as defined by the original authors

Intervention
- Exercise, strengthening, physiotherapy, manual therapy in patients with osteoarthritis of the knee
- Land-based interventions
- Individual or group exercise

Outcomes
- Pain
- Physical function

Comparisons
- Strength training (Code 1) versus nothing/placebo
- Multi-modal exercise (Code 2) versus nothing/placebo
- Exercise plus manual mobilisation (Code 3) versus nothing/placebo
- Comparisons of Code 1, 2 and 3

Figure 1: Inclusion criteria.

Ontwikkeling (EBRO) guideline-development platform [7]. This review included studies scoring three points or greater (Table 1).

Data extraction and analysis

Data were retrieved from the control and intervention groups and included the post intervention scores, standard deviations, and the number of participants. This study used trials that assessed the same outcomes measured in a variety of ways. Consequently, the standardized mean difference was the most suitable measure of effect size. To calculate the standardized mean difference, the difference in the mean outcome between the groups was divided by the pooled standard deviation of the outcome amongst participants [8]. As this statistic does not recognize directional changes where scores measured an outcome in a reverse scale, the mean values were multiplied by -1 [8]. Positive scores indicated the effect was in favor of the intervention group, demonstrating a decrease in pain or an improvement in function. Effect sizes of 0.2–0.5 were considered a small effect, 0.5–0.8 represented a medium effect, and >0.8 a large effect. This was determined in order to keep consistent with a previous similar study and to allow for comparisons [4].

A meta-analysis was conducted to calculate the total effect size for the individual codes for both pain and physical function. None of the trials found in the search appropriately corresponded to Code 3, or directly compared the three codes, therefore it was not possible to conduct an analysis of Code 3. Code 1 and 2 analyses were carried out using Review Manager (RevMan) software (Version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012).

The I^2 statistic is used to measure the consistency between trials in a meta-analysis. In this study, the statistic was used to determine the degree of similarity between the trials within each code, to ensure all studies are evaluating similar effects. I^2 was also used to determine whether the codes were different enough to make worthwhile comparisons [9].

Table 1: Evidence Based Richtlijn Ontwikkeling scores of included studies

Study	RA	CA	SB	PB	TB	AB	DO	ITA	CIR	Total (0 to 9)
Bruce-Brand et al., 2012	Y	N	Y	N	N	Y	N	N	Y	4
Chang et al., 2012	Y	N	Y	Y	N	N	N	N	Y	4
Duman et al., 2012	Y	N	Y	N	N	N	Y	Y	Y	5
Lin et al., 2009	Y	Y	Y	N	N	Y	Y	Y	N	6
Oliviera et al., 2012	Y	Y	Y	N	N	Y	N	Y	Y	6
Rosedale et al., 2014	Y	Y	Y	N	N	Y	N	Y	N	5
Salacinski et al., 2012	Y	N	Y	N	N	N	N	Y	N	3
Salli et al., 2010	Y	Y	Y	Y	N	Y	Y	N	Y	7

Abbreviations: RA= Random allocation, CA= Concealed allocation, SB= Similar at baseline, PB= Participant blinding, TB= Therapist blinding, AB= Assessor blinding, DO= Dropouts (less than 15%), ITA= Intention to treat analysis, CIR= Co-Intervention reported

RESULTS

Figure 2 is a summary of the study selection process. Of the 137 retrieved trials, 16 were relevant. Eight of these studies were excluded as they did not meet the criteria, leaving eight studies which could be included. The 'proprioception' trial arm in one study [10] was excluded because strength training was not a component of this exercise intervention. The multiple trial arms from another study [11] examined two different strength training programs and were therefore considered as two sets of results within Code 1. There were five sets of results included in Code 1 from four studies [10–13] and four sets of results included from four studies in Code 2 [14–17]. Code 3 retrieved no results. One study [18] was excluded from Code 3 because the post-intervention scores did not differentiate between hip and knee OA participants. The principal author was contacted in order to obtain scores for this study, however, access to these scores were unavailable during the data collection period.

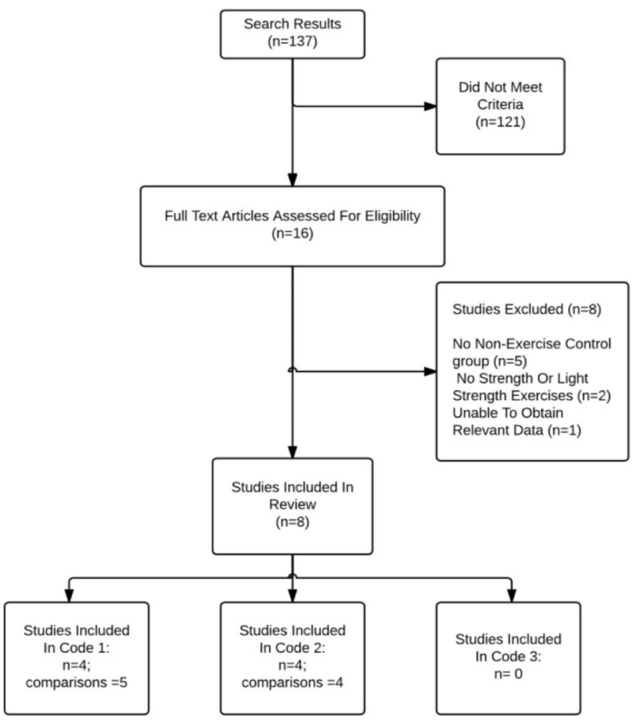

Figure 2: Study selection process.

Study characteristics

The study characteristics are presented in Table 2. Participants had clinical evidence of OA according to either the American College of Rheumatology criteria, or radiographic or arthroscopic evidence. The included trials recruited participants with varying severities of OA, demonstrating a range of Kellgren–Lawrence scores between one and four. The average age of participants in the included studies ranged from 57 to 68 years. All studies recruited predominately female participants except Bruce-Brand et al. [12] whose intervention group had a female to male ratio of 4:6, and 3:3 in the control group. One study had female participants only [13]. The mean percentage of the participants who were female across the studies was 75.6%. The greater representation of females in this study reflects the gender distribution of knee OA, as females are more likely to suffer from the condition [19]. Details of the intervention types are summarized in Table 3. In all included studies, patients continued with standard care both in the intervention and control groups for the duration of the trials. Standard care included a range of interventions such as education, weight loss, pharmacological therapy, transcutaneous electrical nerve Stimulation and heat packs. Most of the studies predominantly used the Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) as a measure of pain and physical function; however, knee injury and osteoarthritis outcome score (KOOS) and the visual analogue scale (VAS) were also used.

Table 2: Summary of included studies

Study	Participants*	Intervention	Outcome measures
Bruce-Brand et al., 2012	n=20 Age = 64 years Gender = 56% male	Exp = home based resistance training exercise program 30 min x 3/week x 6 weeks Individual Con = standard care (OA education, weight loss, pharmacological therapy, physical therapy)	• WOMAC pain • WOMAC physical function • Follow-up = 14 weeks
Chang et al., 2012	n = 41 Age = 68 years Gender = 0% male	Exp = elastic band exercises 30 min x 2–3/week x 8 weeks Con = standard care (physiotherapy, TENS, SWD, hot packs)	• WOMAC pain • WOMAC physical function
Duman et al., 2012	n = 54 Age = 64 years Gender = 9% male	Exp = proprioceptive exercise program (including muscle strengthening, bicycling, walking) ? min x 5/week x 3 weeks Individual Con = NSAIDs, physical therapy (infrared and short wave therapy)	• WOMAC pain • WOMAC physical function
Lin et al., 2009	n=72 Age = 63 years Gender = 31% male	Exp = non weight-bearing strength training – eccentric quadriceps training ? min x 3/week x 8 weeks Individual Con = none	• WOMAC pain • WOMAC physical function
Oliveira et al., 2012	n = 100 Age = 60 years Gender = 6% male	Exp = exercise (stationary bicycle, hamstrings stretching, and quadriceps strengthening) ? min x 2/week x 8 weeks Individual Con = OA instruction manual, ice pack use	• WOMAC pain • WOMAC physical function
Rosedale et al., 2014	n=146 Age = 65 years Gender = 43% male	Exp = individualised directional exercises (end range strengthening), evidence based exercises (quadriceps strengthening, cycling, walking) 20-60 min x 2–3/week x 2 weeks Individual Con = none	• KOOS pain • KOOS function • Follow-up = 3 months
Salacinski et al., 2012	n = 28 Age = 57years Gender = 32% male	Exp = resistance based cycling classes + stretching 40-60 min 2+/week x 12 weeks` Group Con = none	• WOMAC pain • WOMAC physical function
Salli et al., 2010	n concentric/ eccentric = 47 nisometric = 48 Age = 57 years Gender = 18% male	Exp concentric/eccentric = non weight-bearing concentric – eccentric isokinetic exercises Exp isometric = non weight-bearing isometric isokinetic exercises ? min x 3/week x 8 weeks Individual Con = paracetamol	• VAS • WOMAC physical function • Follow-up = 20 weeks

Table only includes arms of data that were analyzed. *All ages and gender variances are participant means as reported by the trials. Abbreviations: Exp = Experimental group interventions, Con = control group interventions, WOMAC = Western Ontario and McMaster Universities Osteoarthritis index, KOOS = Knee Injury and Osteoarthritis Outcome Score, VAS = Visual Analogue Scale

Outcome measures

Pain The effect size for pain demonstrated a large positive effect of 1.26 (95% CI 0.97 to 1.55) for strength training, and a smaller effect of 0.47 (95% CI 0.24 to 0.69) for multimodal exercise therapy (Figure 3). The total combined effect size for codes 1 and 2 was 0.76 (95% CI 0.59 to 1.94)

Physical function The strength training intervention for physical function demonstrated a large positive effect of 1.15 (95% CI 0.87 to 1.44), and a smaller effect of 0.53 (95% CI 0.30 to 0.75) was shown for multimodal exercise therapy (Figure 4). The total combined effect size for codes 1 and 2 was 0.77 (95% CI 0.59 to 0.94).

Table 3: Studies classified by the intervention codes

Study	Treatment	Strength	Aerobic activity	ROM	Stretch	Education	Home exercise program
Code 1							
Bruce-brand et al., 2012	Individual	O				O	O
Chang et al., 2012	Group	O					
Lin et al., 2009*	Individual	O					
Salli et al., 2010 Concentric / Eccentric	Individual	O					
Salli et al., 2010 Isometric	Individual	O					
Code 2							
Duman et al., 2012	Individual	O	O	O			
Oliveira et al., 2012	Individual	O	O	O	O	O	
Rosedale et al., 2014	Individual	O		O		O	
Salacinski et al., 2012	Group	O	O	O	O		

*Strength training intervention arm
Abbreviations: ROM = active range of motion exercises

Comparability

Total effect sizes for pain and physical function were similar, and there was a significant positive correlation between the effects on pain and function (r=0.83, *p*=0.01) (Figure 5). Despite the different interventions in the trials being analyzed, there is some degree of homogeneity within Code 1 (pain: I^2 = 56; function I^2 = 46) and Code 2 (pain I^2 =63, function I^2=47), which allows for comparisons to be made. The subgroup differences between the two codes demonstrated heterogeneity (pain: I^2= 94.5, function: I^2= 91.3) for both outcomes, suggesting that Code 1 and 2 are comparable.

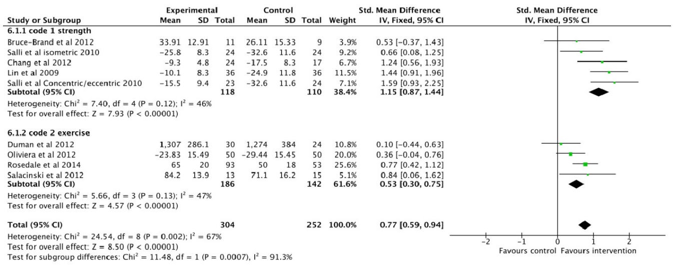

Figure 4: Effect sizes (95% CI) of codes 1 and 2 interventions compared with control for the outcome of physical function.

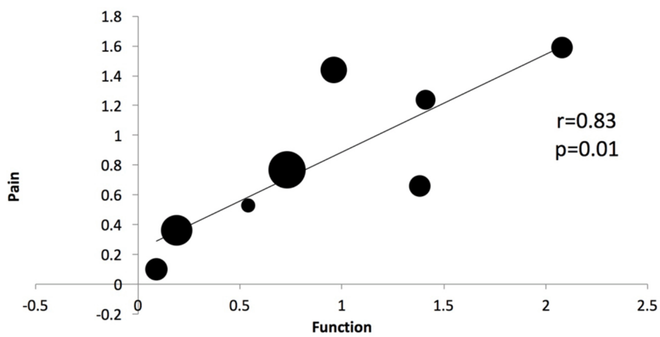

Figure 5: Effect size for pain and function (points drawn proportional to sample size of the studies).

DISCUSSION

This review found that strength training alone and multimodal exercise interventions are both effective in improving pain and function for patients with knee OA, with larger effect sizes demonstrated by strength training alone. As there was a paucity of research on the effects of manual mobilization in conjunction with exercise, it was

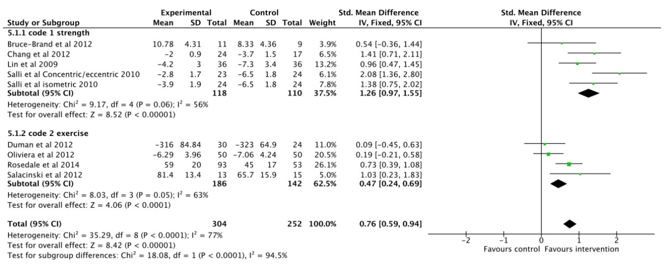

Figure 3: Effect sizes (95% CI) of codes 1 and 2 interventions compared with control for the outcome of pain.

not possible to draw conclusions on the combined effects. Although one study [18] evaluated the effects of manual therapy combined with exercise interventions, the study did not meet the inclusion criteria, and the lack of similar research restricted the capacity for the research question to be answered.

The design of this study was influenced by a systematic review by Jansen et al. [4] which used the same comparisons. However, analyzed earlier studies from 1990 until 2008. Although Jansen et al. [4] demonstrated the same trend for strength training to yield larger effects than exercise therapy for both pain and physical function outcomes, their study produced overall lower effect sizes. Jansen et al. [4] reported that the effect size for pain was 0.38 (95% CI 0.23 to 0.54) for strength training, and 0.34 (95% CI 0.19 to 0.49) for exercise therapy. Jansen et al. [4] also reported effect size for physical function was 0.41 (95% CI 0.17 to 0.66) for strength training and 0.25 (95% CI 0.03 to 0.48) for exercise. We suggested that the discrepancy in effect sizes between the studies could have partly resulted from using different outcome measures. The WOMAC was used in 50% of the trials included in Jansen et al. [4], but in over 80% of trials in this review. The WOMAC provides participants with a greater opportunity to report on improvement, which may in turn influence outcome scores [20]. Other potential reasons for the discrepancy could include the quality of the included studies, dosage, duration and characteristics of exercise interventions.

The benefits of strength training for improving the outcomes of knee OA patients are widely substantiated by literature [2–4, 18, 21]. A 2013 systematic review [2] studied the efficacy of strength training and aerobic exercise on pain relief in people with knee OA. The results demonstrated that strengthening exercises, including weight bearing and non-weight bearing, and aerobic exercises were both effective for pain relief and concluded that non-weight bearing strengthening exercise is the most effective in the short-term. The strength training interventions reviewed in Code 1 predominantly used non-weight bearing exercises, which may provide a reason why the strength training interventions revealed greater effects than multimodal exercise therapy, which tended to include more weight-bearing components. Despite this, the importance of weight bearing exercise on healthy cartilage physiology should also be considered [22]. With the potential for increased pain associated with weight bearing exercise, the authors supported the suggestion made by Tanaka et al. [2] that an integration of weight bearing with non-weight bearing strengthening exercise is optimal, as tolerance for knee joint loading allows. Furthermore, it has been reported that there is a dearth of research on the efficacy of isometric strength training, and it is not possible to draw conclusions on the efficacy [23, 24]. Results from a study included in this review do however add weight to the evidence that isometric strengthening exercise is effective for improvements in pain and function, as well as a reduction in disability and medication usage in knee OA [11].

There was a trend for studies that have more complicated exercise regimes to yield weaker effects. It is hypothesized that this may result from poor compliance, difficult instructions, time constraints or lack of motivation. Code 1 generally incorporated fewer complex exercise programs, thus potentially contributing to the larger effects. Moreover, the results raise questions regarding the art of combining exercise types. A 2013 review highlights the conflicting evidence for mixed exercise programs including strengthening, aerobic, and flexibility components in patients with knee OA [23]. The study suggests that for mixed programs to be effective, each mode of exercise (strengthening, aerobic or range of motion exercises) must meet the minimum requirements for efficacy, and mixed programs tend to be less effective than targeted programs [23]. Mixed programs do, however, support the integration of regular exercise into daily living and encourage improvements in overall wellbeing [23–25].

The inclusion criteria excluded studies involving aquatic activities as well as functional exercise. There is a growing body of evidence to suggest that functional exercises such as yoga and tai chi are effective in the reduction of pain associated with knee OA [23, 26]. Furthermore, there are suggested promising short-term benefits from aquatic exercises, and future research to compare these interventions is warranted [27–29]. Despite the promising nature of these interventions, the exclusion of such studies allowed the results to be homogeneous within the codes. Further research into the long-term benefits of an exercise or manual therapy program for knee OA may also show promise. This review only analyzed the short-term effects. However one included study demonstrated that the benefits demonstrated at 8 week were sustained until 20 weeks for both isometric and concentric/eccentric strength training interventions [11]. Although excluded from this review, a randomized controlled trial evaluating the effects of exercise therapy, manual therapy and a combination of both interventions for hip and knee OA sufferers, revealed that at a one year follow-up, improvements in pain and function were sustained in all three groups [18].

The results of this study could not demonstrate significant comparisons between intervention duration and effect size, however, some studies suggest that beneficial effects of strengthening exercises were influenced by differences in exercise frequency and duration [21, 30]. Tanaka et al. [30] demonstrated that strength training trials longer than ninw weeks were less effective than studies up to eight weeks, however, aerobic trials demonstrated no such correlation between duration and efficacy. A 2008 Cochrane review [21] stated that exercise programs involving more than 12 supervised sessions were associated with greater improvements in pain and function of the knee.

In order to optimize the relevance of knee OA research for clinicians, there is an apparent need to integrate patient focused aspects, such as the presence of comorbidities, multiple joint involvement, sub-grouping of patient presentations, and medication usage into further trials. A point of difference in the study design by Rosedale et al. [16] was their sub-grouping of patients within the exercise group using individuals' response to repeated movements of the knee, leading to a slightly varied exercise focus depending on their response. The study found moderate improvement in pain and function after just two weeks of intervention, which was still evident three months later [16].

The outcome measures in this review focused on pain and physical function. It is believed that these outcomes are most important in measuring knee OA. However, other outcome measures, such as stiffness and quality of life, may also demonstrate useful results [5]. Most of the included studies used a reliable and multifactorial measurement of pain and physical function (WOMAC and KOOS), resultantly activities of daily living have been taken into consideration. Focusing on the outcome of changes in analgesic use may also have clinical relevance due to the increasing health concerns associated with their usage [31]. Salli et al. [11] found reduced intake of analgesic medication in the exercise groups compared to the control group, which appears to be a promising outcome for the wellbeing of OA sufferers. A qualitative analysis of the perceptions of people suffering from OA infer that the analysis of pain should not be restricted to severity and supports the idea of a multifactorial pain scale [20]. These researchers are developing an osteoarthritis symptom inventory scale (OASIS) to assess pain quality. With this movement towards the multifactorial outcome measures, future research should continue to show more clinically applicable results [20].

No studies were retrieved in Code 3. Although this was, in part, due to restrictive inclusion criteria extrinsic factors may have also played a role in explaining why few randomized controlled trials on manual mobilization exist. One study [32] suggested that randomized controlled trials might not be an optimal study design for research of manual therapy interventions. It is suggested that the methods to ensure internal validity of a study, such as randomization and intervention standardization, affect the way in which the results can be applied in a more general context [32]. In turn, this can affect the relevance of the results to clinical practice. By limiting this review to randomized controlled trials we have ensured the inclusion of comparable, high quality studies. However, excluded other study designs such as adaptive clinical trials which could have better reflected individualized interventions as prescribed by health care practitioners.

Several limitations of this study should be noted. The reviewers have defined the control as any intervention without exercise, which may have created a potential for variables to affect the results of the control group. Some of these control group interventions included medication usage, educational pamphlets, ice and heat packs, and transcutaneous electrical nerve stimulation devices. The criteria also did not specify a limitation regarding the severity of knee OA. It was not possible to draw conclusions recommending exercise interventions at specific stages of the disease progression because most of the studies included participants with a wide range of Kellgren–Lawrence scores. Three studies [12, 13, 17] were rated as having low EBRO scores of four or less. These studies had no concealment of allocation, no assessor blinding, more than 15% dropouts, and no intention-to-treat analysis and small sample sizes. Neither the inclusion/exclusion criteria or the EBRO critical appraisal tool took sample size into consideration, allowing for more studies to be included in the review, however, potentially affecting the quality of the included studies.

CONCLUSION

Large effect sizes were found for the strength training intervention for patients with knee osteoarthritis (OA) in both pain and physical function, compared to small to moderate effects for multimodal exercise therapy. It was not possible to draw conclusions from these results regarding the role of manual mobilization as a supplement to therapeutic exercise. However, current literature suggests the adjunctive therapy may be favorable. Further research is required to evaluate the combined effects of manual and exercise therapies. This review has highlighted the importance of the prescription of therapeutic strength exercises in clinical practice. Although results showed that strength training alone compared to multimodal exercise yielded greater improvements in pain and physical function specific to knee OA, other health parameters such as quality of life, cardiovascular health or body weight were not assessed. We are, therefore, not recommending exclusive training of strength alone; rather, we reinforce the importance of incorporating strength training into a rehabilitative exercise regime for people with knee OA.

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Author Contributions

Anna Frances Quillfeldt – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final

approval of the version to be published
Rebecca Melissa Marks – Substantial contributions to conception and design, Drafting the article, Final approval of the version to be published

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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REFERENCES

1. Cross M, Smith E, Hoy D, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis 2014 Jul;73(7):1323–30.
2. Tanaka R, Ozawa J, Kito N, Moriyama H. Efficacy of strengthening or aerobic exercise on pain relief in people with knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. Clin Rehabil 2013 Dec;27(12):1059–71.
3. Uthman OA, van der Windt DA, Jordan JL, et al. Exercise for lower limb osteoarthritis: systematic review incorporating trial sequential analysis and network meta-analysis. Br J Sports Med 2014 Nov;48(21):1579.
4. Jansen MJ, Viechtbauer W, Lenssen AF, Hendriks EJ, de Bie RA. Strength training alone, exercise therapy alone, and exercise therapy with passive manual mobilisation each reduce pain and disability in people with knee osteoarthritis: a systematic review. J Physiother 2011;57(1):11–20.
5. Bellamy N, Kirwan J, Boers M, et al. Recommendations for a core set of outcome measures for future phase III clinical trials in knee, hip, and hand osteoarthritis. Consensus development at OMERACT III. J Rheumatol 1997 Apr;24(4):799–802.
6. Maly MR, Costigan PR, Olney SJ. Determinants of self-report outcome measures in people with knee osteoarthritis. Arch Phys Med Rehabil 2006 Jan;87(1):96–104.
7. Burgers JS, van Everdingen JJ. Evidence-based guideline development in the Netherlands: the EBRO platform. Ned Tijdschr Geneeskd 2004 Oct 16;148(42):2057–9.
8. Higgins JPT, Deeks JJ. Selecting studies and collecting data. In: Higgins JPT, Green S eds Cochrane handbook for systematic reviews of interventions v5.1.0. The Cochrane Collaboration 2011.
9. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003 Sep 6;327(7414):557–60.
10. Lin DH, Lin CH, Lin YF, Jan MH. Efficacy of 2 non-weight-bearing interventions, proprioception training versus strength training, for patients with knee osteoarthritis: a randomized clinical trial. J Orthop Sports Phys Ther 2009 Jun;39(6):450–7.
11. Ulus Y, Tander B, Akyol Y, et al. Therapeutic ultrasound versus sham ultrasound for the management of patients with knee osteoarthritis: a randomized double-blind controlled clinical study. Int J Rheum Dis 2012 Apr;15(2):197–206.
12. Bruce-Brand RA, Walls RJ, Ong JC, Emerson BS, O'Byrne JM, Moyna NM. Effects of home-based resistance training and neuromuscular electrical stimulation in knee osteoarthritis: a randomized controlled trial. BMC Musculoskelet Disord 2012 Jul 3;13:118.
13. Chang TF, Liou TH, Chen CH, Huang YC, Chang KH. Effects of elastic-band exercise on lower-extremity function among female patients with osteoarthritis of the knee. Disabil Rehabil 2012;34(20):1727–35.
14. Duman I, Taskaynatan MA, Mohur H, Tan AK. Assessment of the impact of proprioceptive exercises on balance and proprioception in patients with advanced knee osteoarthritis. Rheumatol Int 2012 Dec;32(12):3793–8.
15. Oliveira AM, Peccin MS, Silva KN, Teixeira LE, Trevisani VF. Impact of exercise on the functional capacity and pain of patients with knee osteoarthritis: a randomized clinical trial. [Article in English, Portuguese]. Rev Bras Reumatol 2012 Dec;52(6):876–82.
16. Rosedale R, Rastogi R, May S, et al. Efficacy of exercise intervention as determined by the McKenzie System of Mechanical Diagnosis and Therapy for knee osteoarthritis: a randomized controlled trial. J Orthop Sports Phys Ther 2014 Mar;44(3):173–81, A1–6.
17. Salacinski AJ, Krohn K, Lewis SF, Holland ML, Ireland K, Marchetti G. The effects of group cycling on gait and pain-related disability in individuals with mild-to-moderate knee osteoarthritis: a randomized controlled trial. J Orthop Sports Phys Ther 2012 Dec;42(12):985–95.
18. Abbott JH, Robertson MC, Chapple C, et al. Manual therapy, exercise therapy, or both, in addition to usual care, for osteoarthritis of the hip or knee: a randomized controlled trial. 1: clinical effectiveness. Osteoarthritis Cartilage 2013 Apr;21(4):525–34.
19. Zhang Y, Jordan JM. Epidemiology of osteoarthritis. Clin Geriatr Med 2010 Aug;26(3):355–69.
20. Cedraschi C, Delézay S, Marty M, et al. "Let's talk about OA pain": a qualitative analysis of the perceptions of people suffering from OA. Towards the development of a specific pain OA-Related questionnaire, the Osteoarthritis Symptom Inventory Scale (OASIS). PLoS ONE 2013;8(11):e79988.
21. Fransen M, McConnell S. Exercise for osteoarthritis of the knee. Cochrane Database of Systematic Reviews 2008;(4):CD004376.

22. Beckwée D, Vaes P, Cnudde M, Swinnen E, Bautmans I. Osteoarthritis of the knee: why does exercise work? A qualitative study of the literature. Ageing Res Rev 2013 Jan;12(1):226–36.
23. Fernandes L, Hagen KB, Bijlsma JW, et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. Ann Rheum Dis 2013 Jul;72(7):1125–35.
24. Smith T, Kirby E, Davies L. A systematic review to determine the optimal type and dosage of land-based exercises for treating knee osteoarthritis Physical Therapy Reviews 2014;19(2):105–13.
25. Escalante Y, Saavedra JM, García-Hermoso A, Silva AJ, Barbosa TM. Physical exercise and reduction of pain in adults with lower limb osteoarthritis: a systematic review. J Back Musculoskelet Rehabil 2010;23(4):175–86.
26. Wang C, Schmid CH, Hibberd PL, et al. Tai Chi is effective in treating knee osteoarthritis: a randomized controlled trial 2009;61(11):1545–53.
27. Bartels EM, Lund H, Hagen KB, Dagfinrud H, Christensen R, Danneskiold-Samsøe B. Aquatic exercise for the treatment of knee and hip osteoarthritis. Cochrane Database Syst Rev 2007 Oct 17;(4):CD005523.
28. Lund H, Weile U, Christensen R, et al. A randomized controlled trial of aquatic and land-based exercise in patients with knee osteoarthritis. J Rehabil Med 2008 Feb;40(2):137–44.
29. Wang TJ, Lee SC, Liang SY, Tung HH, Wu SF, Lin YP. Comparing the efficacy of aquatic exercises and land-based exercises for patients with knee osteoarthritis. J Clin Nurs 2011 Sep;20(17-18):2609–22.
30. Tanaka R, Ozawa J, Kito N, Moriyama H. Effect of the Frequency and Duration of Land-based Therapeutic Exercise on Pain Relief for People with Knee Osteoarthritis: A Systematic Review and Meta-analysis of Randomized Controlled Trials. J Phys Ther Sci 2014 Jul;26(7):969–75.
31. O'Neil CK, Hanlon JT, Marcum ZA. Adverse effects of analgesics commonly used by older adults with osteoarthritis: focus on non-opioid and opioid analgesics. Am J Geriatr Pharmacother 2012 Dec;10(6):331–42.
32. Milanese S. The use of RCT's in manual therapy--are we trying to fit a round peg into a square hole? Man Ther 2011 Aug;16(4):403–5.