# 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

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**Question**: What are the effects of strength training alone, exercise therapy alone, and exercise with additional passive manual mobilisation on pain and function in people with knee osteoarthritis compared to control? What are the effects of these interventions relative to each other? **Design**: A meta-analysis of randomised controlled trials. **Participants**: Adults with osteoarthritis of the knee. **Intervention types**: Strength training alone, exercise therapy alone (combination of strength training with active range of motion exercises and aerobic activity), or exercise with additional passive manual mobilisation, versus any non-exercise control. Comparisons between the three interventions were also sought. **Outcome measures**: The primary outcome measures were pain and physical function. **Results**: 12 trials compared one of the interventions against control. The effect size on pain was 0.38 (95% CI 0.23 to 0.54) for strength training, 0.34 (95% CI 0.19 to 0.49) for exercise, and 0.69 (95% CI 0.42 to 0.96) for exercise plus manual mobilisation. Each intervention also improved physical function significantly. No randomised comparisons of the three interventions were identified. However, meta-regression indicated that exercise plus manual mobilisations improved pain significantly more than exercise alone ($p = 0.03$). The remaining comparisons between the three interventions for pain and physical function were not significant. **Conclusion**: Exercise therapy plus manual mobilisation showed a moderate effect size on pain compared to the small effect sizes for strength training or exercise therapy alone. To achieve better pain relief in patients with knee osteoarthritis physiotherapists or manual therapists might consider adding manual mobilisation to optimise supervised active exercise programs. **[Jansen MJ, Viechtbauer W, Lenssen AF, Hendriks EJM, de Bie RA (2011) 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.** *Journal of Physiotherapy* **57: 11–20]**

**Key words**: Exercise, Physiotherapy, Manual therapy, Osteoarthritis of the knee

## Introduction

Osteoarthritis of the hip or knee is the most common form of arthritis and causes musculoskeletal pain and physical dysfunction. The prevalence of knee osteoarthritis in the Netherlands in 2007 was 14.3 per 1000 for men and 23.8 per 1000 for women, while the prevalence of hip osteoarthritis was 10.2 per 1000 for men and 18.9 per 1000 for women (Poos and Gommer 2009). The disease has a great impact on the patient's physical function and quality of life. Exercise plays an important role in the management of this chronic disabling disease (Zhang et al 2008). An overview of systematic reviews reported that there is high-quality evidence that exercise reduces pain and improves physical function in patients with osteoarthritis of the knee (Jamtvedt et al 2008). Recently, evidence for a positive effect of exercise therapy was provided in a systematic review (Fransen and McConnell 2008). The review showed beneficial effects in terms of both pain (standardised difference in the mean change between the treatment and the control group 0.40, 95% CI 0.30 to 0.50) and physical function (0.37, 95% CI 0.25 to 0.49) in patients with osteoarthritis of the knee

Exercise is a broad concept that may include strength training, range of motion exercises, and aerobic activity. Education and home exercises are also often part of an exercise intervention. Fransen and McConnell (2008) analysed the effects of these various treatment methods, studying subgroup effects for simple quadriceps strengthening, lower limb muscle strengthening, strengthening together with an aerobic component, walking program only, and other treatment content. However, they were unable to demonstrate any significant difference in effect size between these subgroups for either pain or physical function.

For the management of hip and knee osteoarthritis, referral to a physiotherapist is recommended for symptomatic patients (Zhang et al 2007). In the Osteoarthritis Research Society International (OARSI) evidence-based expert consensus guidelines (Zhang et al 2008), the recommendation to refer to a physiotherapist is based on the positive results of studies that analysed the effects of physical therapy (Fransen et al 2001) and manual physical therapy (Deyle et al 2005, Deyle et al 2000). In these studies manual mobilisations were part of the treatment. Physiotherapists and manual therapists frequently combine exercise therapy with passive manual mobilisation to treat impairments

related to joint function. Passive manual mobilisation may include soft-tissue mobilisation and oscillations with the aim of improving joint mobility and joint stability and of relieving pain. Restricted joint mobility, especially in terms of knee flexion, appears to be an important determinant of disability in patients with osteoarthritis (Steultjens et al 2000, Odding et al 1996).

It is not known whether passive manual mobilisations provide additional benefits in terms of reduced pain or increased physical function when compared to strength training or compared to exercise therapy alone. We were unaware of any studies that directly compared these intervention types. Therefore, the purpose of this study was to examine the differential effects of exercise therapy with additional passive manual mobilisation, strength training alone, and exercise therapy alone (combining strength training with active range of motion exercises and aerobic activity) on pain and physical function in patients with osteoarthritis of the knee. The research questions this study tried to answer were:

1. What are the effects on pain and physical function of strength training alone, exercise therapy alone (combining strength training with active range of motion exercises and aerobic activity), and exercise with additional passive manual mobilisation for patients with osteoarthritis of the knee?
2. What are the effects of these interventions relative to each other?

## Method

### Identification and selection of studies

A literature search was performed to identify all eligible randomised controlled trials. Electronic searches of MEDLINE (January 1990–December 2008), PEDro, and CINAHL were performed, using the keywords 'osteoarthritis, knee', 'exercise', 'physical therapy modalities', 'musculoskeletal manipulations' and 'randomised controlled trial', in combination with the recommended search routine for identifying randomised controlled trials (see Appendix 1 on the e-Addenda for the full search strategy). Only full reports in English, French, German, or Dutch were included. On the basis of titles and abstracts, the principal author (MJJ) selected relevant studies, after which two authors (MJJ and AFL) independently selected randomised trials comparing exercise for people with osteoarthritis of the knee versus a non-exercise control group. The inclusion criteria are shown in Box 1. Because the goal was to compare only supervised treatments, we excluded studies that examined home exercise programs as an intervention. Disagreements regarding the suitability of a study for the meta-analysis were resolved by discussion.

### Assessment of study characteristics

*Quality*: Two reviewers (MJJ and AFL) assessed the quality of the studies using criteria from the Evidence Based Richtlijn Ontwikkeling (EBRO) guideline-development platform (AGREE Collaboration 2003, Burgers and van Everdingen 2004). Discrepancies between raters were resolved by discussion.

*Participants*: Studies involving adults with osteoarthritis of the knee, as defined by the original authors, were eligible.

**Box 1.** Inclusion criteria.

Design
- Randomised controlled trial

Participants
- Osteoarthritis of the knee

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

Outcomes
- Measures of pain and physical function

Comparisons
- Strengthening (Code 1) versus nothing/placebo
- Exercise (Code 2) versus nothing/placebo
- Exercise plus manual mobilisations (Code 3) versus nothing/placebo
- Comparisons of three codes

*Interventions*: The studies were categorised as examining one of three intervention types using codes defined by MJ and AFL: 1 = strength training only; 2 = exercise (strength training/active range of motion exercises/aerobic activity); 3 = exercise plus additive manual mobilisations (physio/manual therapy). Inconsistencies in coding were resolved by consensus.

*Outcome measures*: The primary outcomes were pain and physical function. Typical measures of these outcomes include the Western Ontario McMaster Universities Index (WOMAC), the Lequesne Index, and visual analogue scales. Pain and physical function belong to the core set of outcomes for phase III trials in osteoarthritis (Bellamy 1997). Short-term (post-intervention) effects were analysed.

### Data analysis

Outcome measures were extracted by the principal author (MJJ). Two reviewers (MJJ and AFL) extracted information about the different intervention components. For each study and outcome measure, effect sizes were calculated using the difference in the mean change within the intervention and control group divided by the pooled baseline standard deviation. Positive values indicate that the intervention group improved on average more than the control group. Effect sizes of 0.2 to 0.5 can be interpreted as small, 0.5 to 0.8 as moderate, and greater than 0.8 as large effects. To calculate the standard error of the effect size estimates, the pre-test post-test correlation must be known for the pain and function measurements within each study. Since this information was not available for any of the studies, we assumed a correlation of 0.6. All of the analyses were repeated using an assumed correlation of 0.4 and 0.8, yielding essentially identical results.

A meta-analysis was then conducted to obtain the average effect for the different intervention types and to compare these effects against each other. We anticipated that no trials might be found that directly compare any of the three interventions. Therefore we pre-planned a mixed-effects meta-regression model for this purpose, using restricted maximum likelihood estimation to estimate the amount of (residual) heterogeneity and using appropriate dummy variables for the different intervention codes. To examine potential effect modification, we repeated this analysis

including the type of control group (education/usual care/ultrasound vs none), study quality (EBRO score), treatment delivery mode (individual vs group), duration of treatment period (in weeks), treatment frequency per week, duration of treatment period × frequency, sex (% females), mean age of the sample, measurement instrument (WOMAC pain/function vs other) and type of weight bearing exercise used (non-weight bearing, weight bearing, or both) as covariates in the model. All analyses were carried out in R (version 2.10.1) using the 'metafor' package (Viechtbauer 2010).

## Results

### Flow of studies through the review

Of the 153 retrieved trials identified by the literature search, 21 were relevant. Twelve of these relevant studies were randomised controlled trials that met the inclusion and exclusion criteria. Figure 1 outlines the flow of studies through the review. Reasons for exclusion of the studies were: no non-exercise control group (Deyle et al 2005, Diracoglu et al 2005, McCarthy et al 2004, Veenhof et al 2006); no or only light strengthening exercises used in the intervention (Bautch et al 1997, Kovar et al 1992), and not possible to classify under one of the three codes. Two of the studies that could not be classified to one of the three codes best fitted to Code 2 but aerobic activity was lacking (Hopman-Rock and Westhoff 2000, Rogind et al 1998). In the third trial a multimodal physiotherapy program was studied involving taping and massage in addition to exercise (Bennell et al 2005). Moreover aerobic activity was not incorporated in the exercise program. The individual treatment arm in the study of Fransen and colleagues (2001) was excluded because aerobic activity was not incorporated in the exercise program and because heat, ultrasound, laser or interferential therapy were also part of the individual treatment. Moreover the use of manual techniques was not
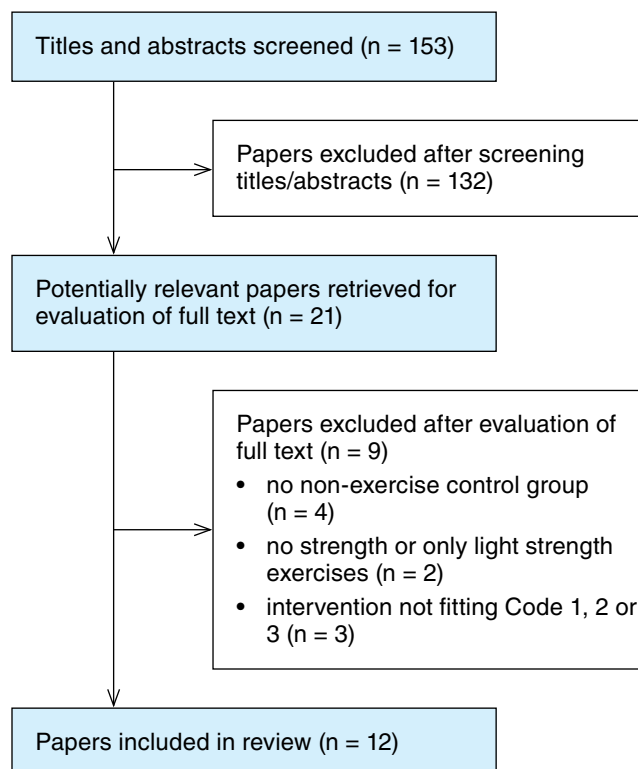


**Figure 1.** Outline of flow of studies through the review.

**Table 1.** EBRO scores of included studies.

| Study | Random allocation | Concealed allocation | Groups similar at baseline | Participant blinding | Therapist blinding | Assessor blinding | <15% dropouts | Intention-to-treat analysis | Co-intervention reported | Total (0 to 9) |
|---|---|---|---|---|---|---|---|---|---|---|
| Baar et al (1998) | Y | Y | Y | N | N | Y | Y | Y | Y | 7 |
| Deyle et al (2000) | Y | Y | Y | N | N | Y | N | Y | N | 5 |
| Ettinger et al (1997) | Y | N | Y | N | N | Y | Y | Y | N | 5 |
| Fransen et al (2001) | Y | Y | Y | N | N | N | Y | Y | N | 5 |
| Hay et al (2006) | Y | Y | Y | N | N | Y | Y | N | Y | 6 |
| Huang et al (2005) | Y | Y | Y | N | N | Y | Y | N | N | 5 |
| Hughes et al (2006) | Y | N | Y | N | N | N | N | N | N | 2 |
| Maurer et al (1999) | Y | N | Y | N | N | Y | Y | N | N | 4 |
| Peloquin et al (1999) | Y | N | Y | N | N | Y | Y | N | N | 4 |
| Schilke et al (1996) | Y | N | Y | N | N | N | Y | N | N | 3 |
| Thorstensson et al (2005) | Y | Y | Y | N | N | N | Y | N | N | 4 |
| Topp et al (2002) | Y | N | Y | N | N | N | Y | Y | N | 4 |

EBRO = Evidence based guideline development (AGREE Collaboration 2003)

**Table 2**. Studies classified by the three intervention codes.

| Study | Treatment | Strength | Aer | ROM | Stretch | Mob p | Manip | Educ | Home |
|---|---|---|---|---|---|---|---|---|---|
| Code 1 | | | | | | | | | |
| Ettinger et al (1997) | Group | ✓ | | | | | | ✓ | ✓ |
| Maurer et al (1999) | Indiv | ✓ | | | | | | ✓ | |
| Schilke et al (1996) | Indiv | ✓ | | | | | | | |
| Topp et al (2002) | Group | ✓ | | | | | | | |
| Huang et al (2005) | Indiv | ✓ | | | | | | | ✓ |
| Code 2 | | | | | | | | | |
| Fransen et al (2001)* | Group | ✓ | ✓ | ✓ | ✓ | | | | ✓ |
| Hay et al (2006) | Indiv | ✓ | ✓ | ✓ | ✓ | | | ✓ | ✓ |
| Peloquin et al (1999) | Group | ✓ | ✓ | | ✓ | | | | |
| Hughes et al (2006) | Group | ✓ | ✓ | ✓ | | | | ✓ | ✓ |
| Thorstensson et al (2005) | Group | ✓ | ✓ | | ✓ | | | | |
| Code 3 | | | | | | | | | |
| van Baar et al (1998) | Indiv | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ | ✓ |
| Deyle et al (2000) | Indiv | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ |

Code 1 = strength exercise, Code 2 = exercise alone (strength exercise/active range of motion exercises/aerobic activity), Code 3 = physio/manual therapy (exercise plus additional manual mobilisations). Fransen* = group therapy arm. Aer = aerobic activity, ROM = active range of motion exercises, Mob p = passive manual mobilisations, Manip = manipulation, Educ = education, Home = home exercise program, Indiv = individual

specified. We were unable to find any study that directly compared any of the three intervention types to each other. Therefore the mixed-effects meta-regression was used to analyse the relative effects of the three interventions.

**Characteristics of studies included**

*Quality*: The methodological quality of the studies ranged from 2 to 7 on a scale from 0 to 9 points. Four studies scored 4 points (Maurer et al 1999, Peloquin et al 1999, Thorstensson et al 2005, Topp et al 2002) and four studies scored 5 points (Deyle et al 2000, Ettinger et al 1997, Fransen et al 2001, Huang et al 2005). The scores of the remaining studies were 2 (Hughes et al 2006), 3 (Schilke et al 1996), 6 (Hay et al 2006), and 7 points (van Baar et al 1998). Table 1 provides an overview of the methodological quality of the included studies.

*Participants*: In 8 of the 12 studies, the participants had clinical evidence of osteoarthritis according to the American College of Rheumatology (ACR) criteria (Altman et al 1986). Two studies recruited patients with radiographic evidence of osteoarthritis. One study used volunteers with osteoarthritis and one study recruited adults older than 55 years who had consulted their general practitioner with pain, stiffness, or both. The mean age of participants in 11 of the 12 studies ranged from 65 to 70 years. In 10 of the 12 studies the majority were female (mean 75%; range 64% to 85%). In one study (Thorstensson et al 2005) mean age was 56 years and 50% were female. In the study of Maurer and colleagues (1999) 58% of the patients were male. Duration of the disease ranged from 5 months to more than 10 years.

*Intervention type*: From one study (Ettinger et al 1997) we took the trial arm that examined resistance training versus a control group. From another study we took the trial arm that examined isokinetic exercise (group I) versus control (Huang et al 2005), and in one study (Fransen et al 2001) we classified the 'group therapy' as Code 2. One study examined two different strength training programs (Topp et al 2002). The mean effects of these programs

were combined and compared with the control group. Six studies were group-based, while the other six used individually delivered treatment. Five studies offered additional education and seven studies incorporated a home exercise program in the intervention. See Table 2 for an overview of the studies included, classified according to the three intervention codes. In five studies the control group received no intervention, whereas in six studies the control group was given education, and in one study therapeutic ultrasound (Deyle 2000). In five of the twelve studies both weight bearing and non-weight bearing strength exercise programs were chosen, while five studies only used non-weight bearing and two only weight bearing strength exercises. See Table 3 for a description of the main aspects of the studies.

*Outcome measures*: Most studies used the WOMAC to analyse the effects on pain and function. Effect sizes could not be calculated for four studies, because standard deviations were missing (Ettinger et al 1997, Maurer et al 1999), total WOMAC scores (instead of the pain and function subscale scores) were presented (Deyle et al 2000), or the results pertained to a mixed group of patients suffering from either hip or knee osteoarthritis (van Baar et al 1998). In the review by Fransen and McConnell (2008), the effect sizes for these four studies were calculated with the help of externally provided data. We used these effect sizes on the assumption that these data had been correctly calculated. We could not retrieve and analyse separate results for patients with knee and hip osteoarthritis from one study (Hughes et al 2006). Generally, effects for knee and hip osteoarthritis have been found to be the same (Jansen et al 2010, van Baar et al 1998), so we used the results for the total group, assuming comparable effect sizes. Finally, for the study by Fransen and colleagues (2001), we assumed that the change between baseline and Week 8 was the same for the two intervention groups. The 16-week results could not be used, since these include control participants that were randomised to the two intervention groups after Week 8.

**Table 3.** Summary of included studies (n = 12).

| Study | Design | Participants | Intervention | Outcome measures |
|---|---|---|---|---|
| Ettinger et al (1997) | RCT | n = 247<br>Age = 69 yr (SD 6)<br>Gender = 30% male | Exp = progressive resistance training (WB/NWB)/home program<br>60 min x 3/wk x 12 wk<br>Group<br>Con = education | • Knee pain scale<br>• Self-reported disability<br>• Follow-up = 3, 9, 18 months |
| Maurer et al (1999) | RCT | n = 98<br>Age = 65 yr (SD 9)<br>Gender = 58% male | Exp = quadriceps isokinetic strength training dynamometer (NWB)<br>? min x 3/wk x 8 wk<br>Individual<br>Con = education | • WOMAC pain<br>• WOMAC function<br>• Follow-up = 8, 12 wk |
| Schilke et al (1996) | RCT | n = 20<br>Age = 66 yr<br>Gender = 15% male | Exp = isokinetic muscle-strength training program (NWB)<br>? min x 3/wk x 8 wk<br>Individual<br>Con = none | • AIMS<br>• Follow-up = 8 wk |
| Topp et al (2002) | RCT | n = 67<br>Age = 63 yr<br>Gender = 26% male | Exp = I: progressive dynamic resistance training (NWB). II: progressive isometric resistance training (NWB)<br>50 min 1/wk x 16 wk<br>Group 1/wk, 2/wk exercise at home<br>Con = none | • WOMAC pain<br>• WOMAC function<br>• Follow up = 16 wk |
| Huang et al (2005) | RCT | n = 62<br>Age = 65 yr (SD 6)<br>Gender = 20% male | Exp = strength training (isokinetic) (NWB). Home exercise program<br>? min x 3/wk x 8 wk<br>Individual<br>Con = none | • VAS pain<br>• Lequesne index<br>Follow-up = 8 wk, 12 months |
| Fransen et al (2001)* | RCT | n = 81<br>Age = 65 yr (SD 7)<br>Gender = 22% male | Exp = strength training (WB/NWB) / 20 min stationary bicycle / home program 3x/wk (stretches followed by 20 min of continuous outdoor walking or indoor stationary bicycle)<br>60 min x 2/wk x 8 wk<br>Group<br>Con = none | • WOMAC pain<br>• WOMAC function<br>Follow-up = 8 wk, 16 wk |
| Peloquin et al (1999) | RCT | n = 124<br>Age = 66 yr<br>Gender = 30% male | Exp = progressive aerobic, strengthening (WB/NWB) and stretching exercises. Aerobic: bicycle progressive to 17 min<br>60 min x 2/wk x 12 wk<br>Group<br>Con = education | • AIMS2<br>Follow-up = 12 wk |
| Hay et al (2006) | RCT | n = 182<br>Age = 68 yr<br>Gender = 35% male | Exp = strength (NWB)/ aerobic / ROM / stretch<br>20 min x 3–6 over a 10-week period<br>Group<br>Con = education | • WOMAC pain<br>• WOMAC function |
| Hughes et al (2006) | RCT | n = 138<br>Age = 73 yr (SD 7)<br>Gender = 16% male | Exp = strength (WB/NWB) / aerobic fitness walking progressive to 30 min / flexibility / education (behaviour change)<br>90 min x 3/wk x 8 wk<br>Group<br>Con = arthritis self-help book | • WOMAC pain<br>• WOMAC function<br>Follow-up = 8 wk, 6 months, 12 months |
| Thorstensson et al (2005) | RCT | n = 61<br>Age = 56 yr (SD 6)<br>Gender = 49% male | Exp = high intensity strength training (WB) / endurance / balance / ergometer cycling 10 min/ home exercise program<br>45 min x 2/wk x 6 wk<br>Group<br>Con = none | • KOOS pain<br>• KOOS ADL<br>Follow-up = 6 wk, 6 months |

**Table 3.** Summary of included studies (n = 12) – continued

| Study | Design | Participants | Intervention | Outcome measures |
|---|---|---|---|---|
| Baar et al (1998) | RCT | n = 113<br>Age = 68 yr<br>Gender = 22% male | Exp = physiotherapy: strength (WB/NWB)/ stretch / aerobic / ROM / co-ordination / manual mobilisations / home exercises / education<br>30 min x 1–3/wk x 12 wk<br>Individual<br>Con = usual care by GP (education plus medication) | • VAS pain<br>• Self-observed disability<br>Follow-up = 12 wk, 24 wk, 36 wk |
| Deyle et al (2000) | RCT | n = 69<br>Age = 61 yr<br>Gender = 43% male | Exp = physio/manual therapy: strength (WB) / stationary bike, 5 min increasing to tolerated time / ROM / stretch / manual mobilisations / home exercises<br>30 min x 2/wk x 4 wk<br>Individual<br>Con = US | • WOMAC<br>Follow-up = 4 wk, 8 wk, 12 months |

Exp = experimental; Con = control; WB = weight bearing; NWB= non-weight bearing; * = group therapy arm

### Effect of intervention types

*Pain*: Figure 2 presents the results for pain. The effect size on pain was 0.38 (95% CI 0.23 to 0.54) for strength training, 0.34 (95% CI 0.19 to 0.49) for exercise therapy, and 0.69 (95% CI 0.42 to 0.96) for exercise therapy plus manual mobilisation. On the meta-regression, only the difference between exercise therapy and exercise therapy with additional manual mobilisation was significant ($p = 0.03$), although the difference between strength training and exercise therapy with additional manual mobilisation was close to being significant ($p = 0.06$).

*Physical function:* The effect size on physical function was 0.41 (95% CI 0.17 to 0.66) for strength training, 0.25 (95% CI 0.03 to 0.48) for exercise and 0.43 (95% CI 0.05 to 0.81) for exercise therapy with additional manual mobilisations (see Figure 3). With meta-regression, no significant differences were found between the effect sizes of the different interventions with respect to physical functioning.

Generally, the effect sizes for function tended to be smaller than those for pain (see Figure 4). Nevertheless, a positive significant correlation was found between the effects for pain and function, ($r = 0.78$, $p = 0.003$).
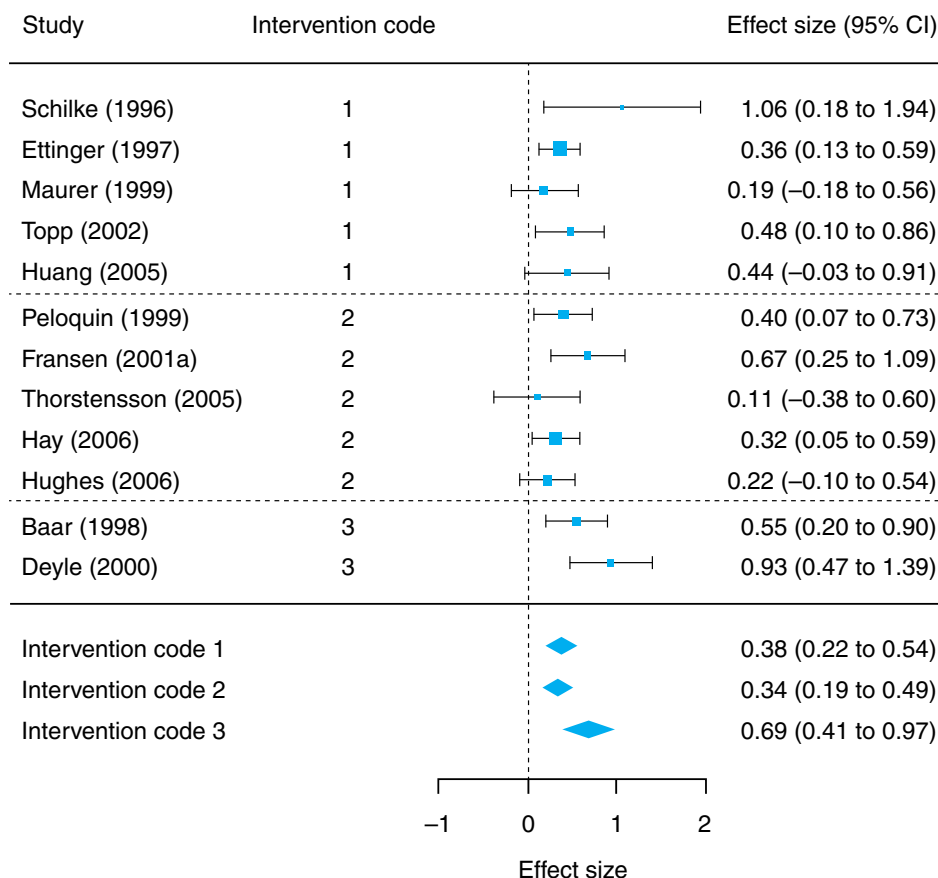


**Figure 2.** Effect sizes (95% CI) of the three intervention codes on pain compared with control.

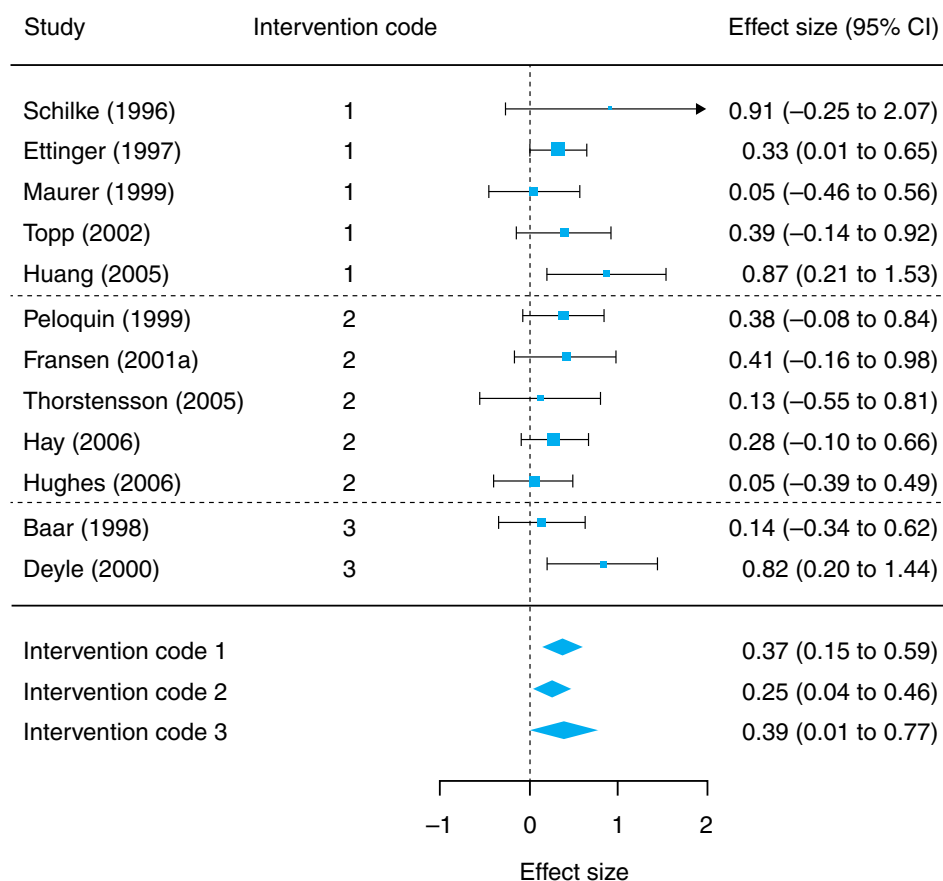| Study | Intervention code | | Effect size (95% CI) |
|---|---|---|---|
| Schilke (1996) | 1 | | 0.91 (−0.25 to 2.07) |
| Ettinger (1997) | 1 | | 0.33 (0.01 to 0.65) |
| Maurer (1999) | 1 | | 0.05 (−0.46 to 0.56) |
| Topp (2002) | 1 | | 0.39 (−0.14 to 0.92) |
| Huang (2005) | 1 | | 0.87 (0.21 to 1.53) |
| Peloquin (1999) | 2 | | 0.38 (−0.08 to 0.84) |
| Fransen (2001a) | 2 | | 0.41 (−0.16 to 0.98) |
| Thorstensson (2005) | 2 | | 0.13 (−0.55 to 0.81) |
| Hay (2006) | 2 | | 0.28 (−0.10 to 0.66) |
| Hughes (2006) | 2 | | 0.05 (−0.39 to 0.49) |
| Baar (1998) | 3 | | 0.14 (−0.34 to 0.62) |
| Deyle (2000) | 3 | | 0.82 (0.20 to 1.44) |
| Intervention code 1 | | | 0.37 (0.15 to 0.59) |
| Intervention code 2 | | | 0.25 (0.04 to 0.46) |
| Intervention code 3 | | | 0.39 (0.01 to 0.77) |

**Figure 3.** Effect sizes of the three intervention codes on physical function compared with control.
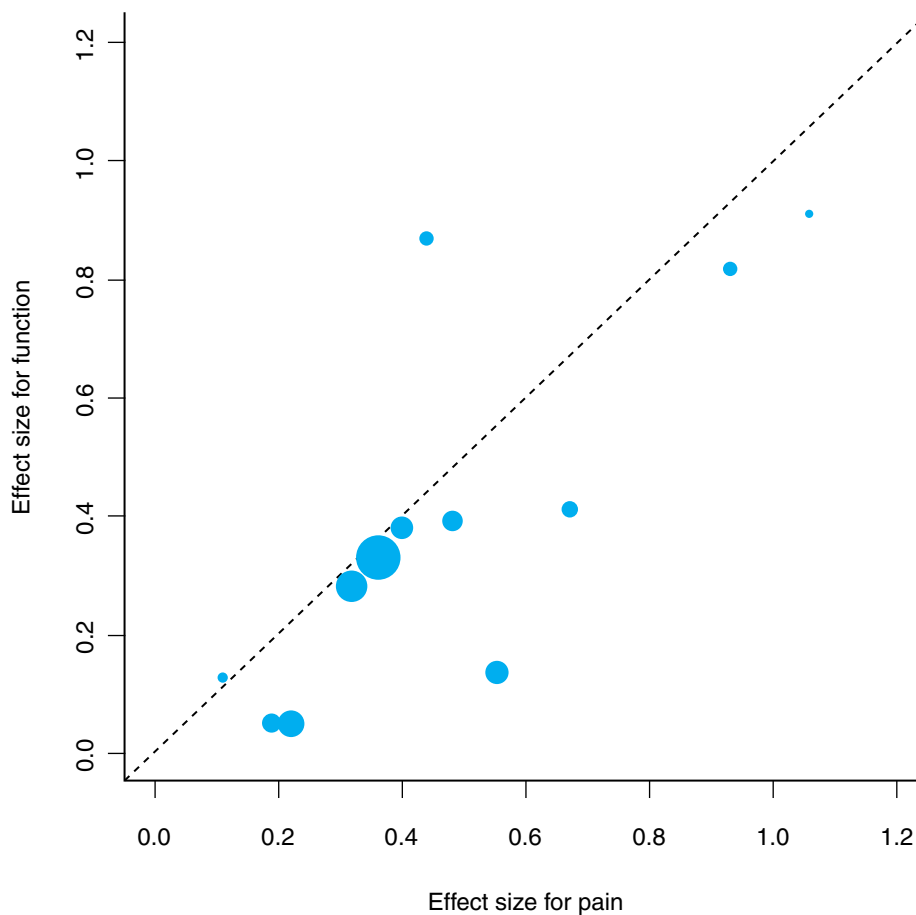


**Figure 4.** Effect sizes for pain and function (points drawn proportional to the sample size of the studies).

The test for residual heterogeneity was not significant for pain ($Q_E$(df = 9) = 9.93, $p$ = 0.36), but it was for function ($Q_E$(df = 9) = 18.22, $p$ = 0.03). Moderator analyses showed that none of the potential covariates (control group, study quality, treatment delivery mode, duration of treatment period, treatment frequency, duration of treatment period × frequency, sex, age, measurement instrument, and type of weight bearing exercise) had a significant influence on the size of the effects for pain or function.

## Discussion

All three intervention types were effective at relieving pain and improving physical function. The effect size of exercise with additional manual mobilisation on pain (0.69) could be considered of moderate size, while the effect sizes of strength training (0.38) and exercise therapy alone (0.34) could be considered small. The effects on physical function tended to be smaller than those on pain, and would be considered moderate or small. Compared to the review by Fransen and McConnell (2008), our calculated effect sizes are somewhat lower, both for strength training and for exercise therapy (strength training in combination with active range of motion and aerobic exercises). This may be related to the fact that we used a different classification procedure and did not incorporate home exercise programs. Nevertheless, confidence intervals in our study were relatively narrow, especially for pain, suggesting sufficiently reliable effect sizes. For exercise with additional manual mobilisation only two studies were included, resulting in larger confidence intervals and less reliable effect sizes.

The treatments categorised to one of the three intervention types may differ in the regimen in which they were applied. None of the variables we examined, such as duration of treatment period and frequency, had a significant influence on the size of the effect. Also, whether the exercise is weight bearing was not an influencing factor, confirmed by equally significant improvements after weight bearing exercise and non-weight bearing exercise (Jan et al 2009). But the results may be influenced by other factors, such as kind of progression, therapy loyalty, or type of aerobic exercise. In most of the studies stationary bike was part of the treatment and in one study aerobic fitness walking (in two studies the type of aerobic exercise was not specified). It is not known if these aerobic exercises have different effects for pain or physical function. Another possible influencing factor is additional co-ordination and postural control exercise that was applied in two studies, one categorised to exercise (Thorstensson et al 2005) and one to physio/manual therapy (van Baar et al 1998). One study investigated this topic and found significant better effects of strength training with additional kinesthesia and balance exercises compared to strength training alone for the functional capacities of patients, but not for pain (Diracoglu et al 2005).

The results of this review are limited to short-term effects. Only five of the studies we included also assessed long-term effects (after 6 months or one year) (Deyle et al 2000, Ettinger et al 1997, Huang et al 2005, Hughes et al 2006, van Baar et al 1998). Four of these studies found effects fading to some extent in the long term, while one study (Huang et al 2005) found results persisting to the end of the one-year follow-up period. It is always a challenge to maintain effects in the long term, but we do not know which treatment method offers the most sustainable results. Well-designed self-management programs and/

or booster sessions (Pisters et al 2007) may help patients keep up exercising and remain active. We agree with the recommendation that patients with osteoarthritis of the knee should be encouraged to undertake and continue to undertake regular aerobic, muscle strengthening, and range of motion exercises (Zhang et al 2008).

The effect size of exercise with additional manual mobilisation on pain was significantly higher than that of exercise therapy alone. Since our review provides only an indirect comparison between the different treatment types, it is not possible to conclude with certainty which treatment program is superior. We were unable to find any study that directly compared these intervention types. There has been one trial that compared a home exercise program with exercise plus additional manual mobilisation (Deyle et al 2005) and concluded that manual therapy combined with supervised exercise offers greater symptomatic relief. For osteoarthritis of the hip, it was found that manual therapy (focusing on traction, or manipulation, and stretching) resulted in greater improvement in terms of pain and physical function than exercise (which focused on exercise strength and range of motion) (Hoeksma et al 2004). Two new trials are currently planning to investigate the effectiveness of physiotherapy programs that incorporate exercise and manual therapy for the management of pain and disability in adults with osteoarthritis of the hip or knee (Abbott et al 2009, French et al 2009).

Despite the limitations of the review, it suggests that additional manual mobilisations may have significantly better effects compared to exercise alone in terms of pain relief. The manual mobilisation techniques used in two studies (Deyle et al 2000, van Baar et al 1998) involved muscle stretching exercises (Evjenth and Hamberg 1988) and passive physiologic and accessory joint movements and soft tissue mobilisation (Maitland 1991, Mink et al 1983) to diminish pain and improve range of motion. From a biomedical perspective, it seems reasonable that manual techniques could be useful especially for pain because the oscillations (eg, in traction degrees I and II) are intended to induce pain inhibition. Furthermore, the purpose of manual mobilisation techniques is to restore damaged periarticular and intra-articular connective tissue. Deyle and colleagues (2000) suggested that periarticular and muscular connective tissue could be implicated as symptom sources in patients with osteoarthritis of the knee. One (pilot) study analysed the effect of knee joint mobilisation on osteoarthritic hyperalgesia and found favourable effects on pain (Moss et al 2006). In our opinion, additional manual mobilisation is an effective adjunct to exercise in physiotherapy for patients with pain from osteoarthritis of the knee.

The exercise protocols used in the studies included in the present review recommended manual mobilisations for patients with a lot of pain and with restricted range of motion (Fransen et al 2001, van Baar et al 1998). In the study by Deyle and colleagues (2000), the treatment group received manual physical therapy based on the results of the examination. We hypothesise that larger effects of manual mobilisations can be expected specifically in subgroups of patients with more pain, greater loss of mobility, or both. Neither of the two studies categorised as examining physio/manual therapy described how often additional passive manual mobilisations were delivered. A cohort study that measured the process of care in physiotherapy treatment according to the Dutch guidelines on osteoarthritis of the

hip and knee found that the proportion of passive manual mobilisations in physiotherapy treatment was 18% (Jansen et al 2010).

Higher effects on pain tend to be paired with higher scores on physical function because the relationship between the effects for pain and physical function was fairly strong (r = 0.78). Similarly, in a cross-sectional survey it was found that in men and women with knee osteoarthritis pain intensity during the last eight days was significantly associated with WOMAC physical function (Perrot et al 2009). In a 3-year cohort study, increased pain was found to be associated with worsening of limitations in activities in patients with osteoarthritis of the hip or knee (van Dijk et al 2006). So, for many patients with osteoarthritis of the knee it is suggested that pain relief is accompanied by improvements in functioning.

In conclusion, exercise therapy plus manual mobilisation showed a moderate effect size on pain (0.69) compared to the small effect sizes for strength training (0.38) or exercise therapy alone (0.34). Supervised exercise treatment in physiotherapy and manual therapy should in our opinion include at least an active exercise program involving strength training, aerobic activity exercises, and active range of motion exercises. To achieve better pain relief in patients with knee osteoarthritis, physiotherapists or manual therapists might consider adding manual mobilisation to optimise supervised active exercise programs. More evidence is needed to examine the short- and long-term effects of adding passive manual mobilisation specifically in subgroups of patients with more pain, greater loss of mobility, or both. ∎

*eAddenda*: Available at JoP.physiotherapy.asn.au
Appendix 1

*Competing interests*: None declared.

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