

Fransen M, McConnell S, Hernandez-Molina G, and Reichenbach S. Exercise for osteoarthritis of the hip (Review). *Cochrane Database of Systematic Reviews* 2014, Issue 4.

Design: Meta-analysis of randomized clinical trials

Date: 3-4-15 LM

Reviewed (2-13-17): No changes to conclusions LM

Study Question: To determine whether land-based therapeutic exercise is beneficial for people with hip OA in terms of reduced joint pain and improved physical function and quality of life.

PICOs:

- **Patients:** Participants 18 years of age or over with clinical radiologic confirmation of hip osteoarthritis (OA) as defined using accepted criteria or self-reported hip OA based on chronic anterior joint pain.
- **Interventions:** Any land-based therapeutic exercise regimens aiming to relieve the symptoms of hip OA, regardless of content, duration, frequency or intensity. This includes any exercise designed to improve muscle strength, range of joint movement or aerobic capacity (or combinations of the 3) and could be supervised or designed as a home program. It includes pre-surgery programs.
- **Comparison interventions:** The control group could be active, including any non-exercise intervention or placebo, including a no treatment or waiting list group.
- **Outcomes:** Each RCT needed to include assessment of at least one of:
 - hip pain;
 - self-reported physical function;
 - quality of life.Each outcome was assessed at two time points: immediately at the end of treatment (post-treatment) and long-term follow-up. If data on more than one pain or physical function scale were reported in a trial, data were extracted from the scale according to a pre-determined hierarchy of outcome scales.
- **Study types:** Randomized controlled trials (RCTs) or controlled clinical (quasi-randomized) trials comparing some form of land-based therapeutic exercise with a non-exercise group.

Study selection:

- Databases included MEDLINE, EMBASE, CINAHL, PEDro, and the Cochrane Library through February 2013. Also searched were ClinicalTrials.gov and the WHO trials portal.
- Three review authors independently assessed articles on trial quality for inclusion and resolved any disagreements through consensus or consulting a fourth review author. The three authors independently extracted data from included studies and assessed articles for risk of bias, with 3 levels of quality of evidence; low risk, high risk or unclear risk.
- Risk of bias was assessed using the Cochrane Collaboration 'risk of bias' tool which uses the following criteria; random sequence generation, allocation concealment,

- blinding of participants, providers, and outcome assessors, incomplete outcome data, selective outcome reporting, and other potential sources of bias.
- If the random sequence generation, allocation concealment, and incomplete outcome data domain were adequately met in a study, the overall risk of bias was judged as low for that study.
 - As the studies used a variety of continuous scales to measure pain and physical function, a unitless measure of treatment effect size was needed to allow the results of the various RCTs to be pooled. Standardized mean differences (SMD) were used to calculate treatment effect sizes from the end of treatment scores and related standard deviation (SD) scores, and to obtain a summary estimate.
 - Heterogeneity in meta-analysis was assessed with the I^2 statistic. Data was pooled and outcomes combined using the random-effects model for a meta-analysis. If $I^2 \geq 30\%$ and $\leq 60\%$, this represented moderate heterogeneity, while I^2 greater than 50% was considered as representing substantial heterogeneity.
 - Subgroup analyses were planned to assess for potential small-study bias in the meta-analyses by comparing effect estimates derived from a random-effects model and a fixed-effect model.
 - The minimal clinically important difference (MCID) for each outcome was determined to be 15 points on a 0- to 100-point pain scale, and 10 points on a 0- to 100-point function scale.
 - A sensitivity analysis was planned to evaluate potential exercise program targeting in order to assess the impact of recruiting solely participants with hip OA compared with recruiting participants with hip or knee OA.

Results:

- Five new studies since the last update in 2009 were included in this update.
- Overall 10 studies with 549 participants with mostly mild-to-moderate symptomatic hip OA, alone or with knee OA were included. Only two RCTs had more than 50 participants in each allocation.
- There was large variability in treatment dosage. Four studies provided fewer than 10 supervised exercise sessions and 5 studies provided at least 16 sessions. Six of the 10 RCTs evaluated class-based programs, while the other 4 studies provided treatments as individual sessions with a physiotherapist.
- Nine studies evaluated more traditional muscle strengthening, functional training and aerobic fitness programs, and one study evaluated a specific 'Tai Chi for Arthritis' program.
- Symptom duration varied among study participants from less than one year to already on the surgery waiting list.
- For pain and physical function, 9 RCTs provided immediate post-treatment outcomes assessments, while 5 RCTs evaluated long term follow-up three to six months after completion of the supervised exercise program.
- Seven of the 10 included RCTs were assessed as 'low risk of bias' for allocation concealment while three had 'uncertain risk'. None of the included RCTs were able to blind participants or therapists providing the interventions to treatment allocation. All of the included RCTs reported blinding of the outcomes assessor.

- Nine RCTs were included in the meta-analysis for the immediate post-treatment pain outcome with 549 participants.
- Nine RCTs were included in the meta-analysis for the immediate post-treatment function outcome with 521 participants.
- There was high-quality evidence from 9 studies (549 participants) that showed that exercise does have a statistically significant beneficial effect for patient pain reduction immediately after treatment (SMD) -0.38, 95% (CI) -0.55 to -0.20). The mean pain after treatment in the control group was 29 points, and 21 points in the exercise group on a 100 point pain scale. The mean difference was 8 points lower with decreased pain in the exercise group (95% CI 4 to 11 points). This equates to a 28% relative improvement. This effect size would be considered small to moderate. Between-study heterogeneity was negligible ($I^2 = 0\%$).
- There was high-quality evidence from 9 studies (521 participants) that showed that exercise does have a statistically significant beneficial effect on patient function immediately after treatment (SMD) -0.30, 95% (CI) -0.54 to -0.05). The mean physical function after treatment in the control group was 29 points, and 22 points in the exercise group on a 100 point function scale. The mean difference was 7 points lower with improved function in the exercise group (95% CI 1 to 12 points). This equates to a 24% relative improvement. This effect size would be considered small to moderate. Between-study heterogeneity was moderate ($I^2 = 41\%$).
- The reduction in pain was sustained at least three to six months after ceasing monitored treatment. There was high-quality evidence from 5 studies (391 participants) that showed that exercise does have a statistically significant beneficial effect for patient pain reduction 3 to 6 months after treatment (SMD) -0.38, 95% (CI) -0.58 to -0.18). The mean pain after treatment in the control group was 29 points, and 21 points in the exercise group on a 100 point pain scale. The mean difference was 8 points lower with sustained reduction in pain in the exercise group (95% CI 4 to 12 points). This equates to a 28% relative improvement. This effect size would be considered small to moderate. Between-study heterogeneity was negligible ($I^2 = 0\%$).
- The improvement in physical function was also sustained for 3 to 6 months after exercise treatment. There was high-quality evidence from 5 studies (365 participants) that showed that exercise does have a statistically significant beneficial effect on patient function 3 to 6 months after treatment (SMD -0.37, 95% CI -0.57 to -0.16). The mean physical function after treatment in the control group was 24 points, and 17 points in the exercise group on a 100 point function scale. The mean difference was 7 points lower with improved function in the exercise group (95% CI 4 to 13 points). This equates to a 24% relative improvement. This effect size would be considered small to moderate. Between-study heterogeneity was negligible ($I^2 = 0\%$).
- Only five of the 10 RCTs exclusively recruited people with symptomatic hip OA (419 participants). There was no significant difference in pain or physical function outcomes compared with 4 studies recruiting participants with either hip or knee OA (130 participants). However, participants recruited with either hip or knee OA demonstrated a larger reduction (not significantly different) in mean pain (SMD -0.66, 95% CI -1.02 to -0.29) than those recruited with only hip OA (SMD -0.30, 95% CI -0.49 to -0.10).

- Of the five studies reporting adverse events, each study reported only one or two events, and all were related to increased pain attributed to the exercise program.

Authors' conclusions:

- The overall results of the meta-analysis (high-level evidence) suggest that land-based exercise is beneficial in terms of reduced pain and improved physical function at the completion of a supervised exercise program and these benefits are sustained for at least a further three to six months among people with symptomatic hip OA. The level of pain was generally mild to moderate at baseline and although the reduction in pain in favor of exercise was potentially small (a mean absolute change of 8%), a mean relative change of 28% (38% for the upper limit) could be considered clinically important for a low risk intervention such as exercise. Similarly for physical function, a relative change of 42% could not be ruled out.
- Most of the RCTs included in this systematic review were considered to have a 'low risk of bias'. While all the RCTs reported having blinded outcome assessment, participants were aware of their allocation status. Given that the main outcomes of this review were participant self-reported pain and physical function, there is a possibility that the treatment effect sizes may be inflated. Given the difficulty blinding participants to exercise treatment allocation (versus no exercise) and the high quality of the evidence for pain and physical function benefit, it is expected that new studies would not change the confidence in the effect estimates.
- The quality of the body of evidence was high for the outcomes of pain and function. Although there may be a potential study limitation for the evidence for pain and function (a potential for bias that may overestimate the effect sizes), it was not considered substantial enough to downgrade the evidence.
- Future studies should explore the effect of more intensive lower limb muscle strengthening programs and provide more information on the effect of strategies to improve exercise adherence in this population. This review included only five studies specifically targeting people with hip OA. A larger number of multi-armed randomized studies would allow for meaningful subgroup analyses to help provide evidence for optimal exercise content, protocols, and dosage. In addition, future research should assess the long-term effectiveness of exercise for people with hip osteoarthritis in terms of disease progression and time to joint replacement surgery.

Comments:

- The mean effect size for immediate post-treatment hip pain reported in this meta-analysis was similar to those reported in a previous meta-analysis (SMD -0.38) (Hernandez-Molina 2008).
- The original Cochrane review, "Exercise for osteoarthritis of the hip" (Fransen 2009), could only pool the findings of five RCTs with 204 participants. This previous review did not demonstrate a significant benefit in terms of pain and physical function. Marked heterogeneity was evident and only one of the five RCTs restricted recruitment to people with hip OA. In the current review, about 75% of study

participants or 5 of 10 RCTs restricted recruitment to people with hip OA. The higher proportion of RCTs restricting recruitment to people with hip OA for this update may explain the shift to finding significant improvement for physical function in the current update. It behooves us to interpret the hip/knee literature with caution when looking for evidence on the hip alone related to OA and exercise.

- The three larger RCTs demonstrating significant benefits were among the five RCTs that restricted recruitment to people with hip OA only. It is likely that their exercise programs were more specific to the hip compared to RCTs that recruited both people with knee, hip or both knee and hip OA. This is particularly concerning for hip OA, since the proportion of participants with hip OA in these combined programs is always much smaller than the proportion with knee OA, and so the combined exercise programs may be more geared to the participants with knee OA.
- There were marked differences between the 10 included RCTs in the content and duration of the exercise programs provided. In 3 of the largest RCTs that demonstrated significant benefits, a total of 8, 16, and 24 exercise sessions were provided over 8 to 12 weeks. Two of these RCTs offered individually supervised sessions with a physiotherapist. One RCT included muscle strengthening and functional exercise, another included high-intensity muscle strengthening, and the third prescribed a daily home program for 30 minutes of walking, cycling, or swimming. These extreme differences in treatment dosage and duration make it impossible to develop recommendations for effective treatment.
- Seven of the 10 included RCTs had a low risk of bias. However, all the results may be vulnerable to performance and detection bias, since none of the RCTs were able to blind participants to treatment allocation, and the outcomes of pain and physical function were participant self-reported. Effect sizes may also be inflated.
- Only four of the 10 included RCTs indicated evidence of study registration. In addition, unpublished studies were not searched. The possibility of publication bias could not be ruled out.
- One included RCT was only reported as a conference abstract with insufficient information to evaluate risk of bias criteria. This abstract should not have been included in this Cochrane Review, because it is clearly low quality evidence (Carlson 2011). It had high or unclear risk of bias in all 7 domains. It was wise of the authors to exclude this RCT from the pooled meta-analyses.
- The minimal clinically important difference (MCID) for each outcome for this meta-analysis was determined to be 15 points for pain, and 10 points for function. This meta-analysis did display statistically significant results for both pain and function, but did not attain clinically important results overall. The difference in pain reduction and functional improvement was only 8 and 7 points, respectively, for both immediate and sustained effect. However, these small clinically insignificant benefits seen here still could be considered a clinically important benefit for a low risk intervention such as exercise. Even though exercise improved physical function by only 7 points post-treatment (95% CI =1-12 pts) and again 3 to 6 months after treatment (95% CI = 4 to 13 pts), the confidence intervals encompass the clinically important difference of 10 points, indicating a very small, but clinically important effect. Larger trials are needed to confirm whether effects shown in the trials included in this review actually confer clinically important benefits.

Assessment:

- High quality Cochrane meta-analysis which supports strong evidence that land-based exercise shows a small clinically important benefit for the relief of pain and improvement in function at the completion of a supervised exercise program and these benefits are sustained for at least another three to six months among people with symptomatic osteoarthritis of the hip.

References:

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- Hernandez-Molina G, Reichenbach S, Zhang B, Lavalley M, Felson DT. Effect of therapeutic exercise for hip osteoarthritis pain: results of a meta-analysis. *Arthritis and Rheumatism* 2008;**59**:1221–8.
- Carlson NL, Christopherson Z, Arnall E, Mohn S, Holton K, Marshall L, et al. A pilot study of the effects of strength and aerobic conditioning in patients with hip osteoarthritis. *Osteoarthritis and Cartilage* 2011;**19**:S212.