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REVIEW ARTICLE

# Effects of group-based versus individual physical exercise programs for knee osteoarthritis: A systematic review and meta-analysis

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**Abstract**

**Background**: Knee osteoarthritis (OA) is the most common joint disease worldwide and is associated with a high rate of disability and poor quality of life. However, little is known about the therapeutic effects of group-based versus individual-based physical exercise protocols. **Objective:** To investigate the effects of individual versus group-based physical exercises on pain intensity and functional outcomes in people with knee OA. **Methods:** MEDLINE/PubMed, Cochrane, EMBASE, and PEDro databases were searched from the earliest date available to July 2023. Study quality was evaluated using the PEDro scale. Mean difference (MD), standardized mean difference (SMD), and 95% confidence interval (CI) were calculated using a random effect model. **Results:** Six studies, with 763 patients, met the study criteria. Group-based physical exercises improved pain intensity (VAS 0-100) MD -17.2 (95% CI: -22.2 to -12.3), the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale MD -0.54 (95% CI: -1.0 to -0.08), WOMAC function subscale MD -2.1 (95% CI: -4.1 to -0.08) compared to individual modality. No significant difference regarding muscle strength and exercise tolerance was found for participants in the group-based physical exercises compared with individual physical ones. **Conclusion:** Group-based physical exercise was more successful in reducing pain intensity and functional impairment in patients with knee OA than individual exercise programs. Both group-based and individual physical exercise programs enhanced muscle strength and 6-minute walk distance.

**Keywords**: Knee osteoarthritis; physical exercises; pain intensity.

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## BACKGROUND

Weight gain is a common concern for midlife women and has been reported in several studies. In the Study of Women Across the Nation (SWAN), midlife women (n=3064) gained an average of 0.7 kg per year, independent of age at baseline or menopause status[1]. Although racial and socioeconomic disparities impacted body weight at baseline (i.e., non-white and lower socioeconomic status are associated with higher baseline weight), subsequent studies showed that weight gain occurred across all midlife women, suggesting the uniformity of this trend[2]. However, weight gain is not limited to midlife; numerous studies have documented an average yearly weight gain of 0.5 kg to 1 kg in US adults[3,4]. Obesity is a critical condition characterized by an accumulation of body fat resulting in body weight that is at least 20% more than the optimum weight[5].

Knee osteoarthritis (OA) is the most common joint disease, with high disability rates and poor quality of life[1]. A Global Burden of Disease study reported that 9.6 million years lived with disability (YLDs) were lost due to hip and knee OA in 2017[2,3]. Thus, improving awareness of risk factors, the need and advantages of treating OA, and providing health services to persons with OA are essential to controlling the condition's future burden[3]. Physical exercises have usually been employed in rehabilitation to address knee OA for nearly a century[4,5], given their effectiveness against this debilitating rheumatic disease[4-6].

Individual exercise programs (known as one-to-one exercise therapy) are widely used in most rehabilitation areas[7]. Studies have suggested that individual therapy programs provide more remarkable outcomes for patients, as they receive intervention within a program that can be individually tailored to meet their needs[7,8]. A study addressed patients' and physical therapists' perceptions regarding factors influencing patient-therapist interactions and found that individualized patient-centered care (i.e., individualizing the treatment to the patient and taking the patient's opinions into account) was one of the most important aspects[9]. Despite beneficial effects, individual physical exercise programs can be expensive[8].

On the other hand, group-based physical exercise interventions are typically less costly than individual therapy. Also, group-based physical exercise has some advantages, such as a supportive and motivating environment, since social interaction is positive for providing peer support, increasing motivation, and opportunities to reduce social isolation. It is also known that social interaction with others and engaging in physical activity releases endorphins, which can improve mood and reduce feelings of isolation. Moreover, participants can try different activities to prevent exercise monotony and help target various muscle groups. This strategy can improve patients' time engagement in activity, leading them to better functional outcomes[7].

Nevertheless, no systematic review or meta-analysis has compared group-based versus individual physical exercises to reduce pain intensity and improve functional outcomes in people with knee OA. Thus, this study aimed to perform a comprehensive systematic literature review and meta-analysis of randomized controlled trials (RCTs) to investigate the effects of group-based versus individual physical exercise programs to reduce pain intensity and improve functional outcomes in people with knee OA.

## METHODS

This systematic review and meta-analysis (PROSPERO: ID CRD42022354077) was performed following Cochrane recommendations[10] and reported under the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline[11].

### Eligibility Criteria

RCTs were eligible if they met the following criteria: I) Participants: persons aged ≥ 18 years with knee OA; II) Intervention: studies with group compared to individual physical exercise intervention or control (no exercise/usual care); III) Outcomes: pain and physical-functional outcomes (physical function, muscle strength, balance, mobility, exercise tolerance); IV) Study design: RCTs.

**Search methods for identification of studies**

EMBASE, MEDLINE/PubMed, Physiotherapy Evidence Database (PEDro), and the Cochrane Central Register of Controlled Trials (CENTRAL Cochrane) were searched up to July 2023 without language restriction. A standard protocol and, whenever possible, a controlled vocabulary (Emtree for EMBASE and Mesh term for PubMed/ Cochrane library) were used for this study. Three groups of keywords and their synonyms (study design, participants, and intervention) were used for the search strategy.

The strategy developed by Higgins et al.[10] was used to screen studies in databases. The search strategy adopted in this study for PubMed, Cochrane, and EMBASE can be found in Supplementary Material 1. Similar search terms were used to identify additional studies in other databases. The references from the included studies were checked to identify other potentially eligible references.

**Data collection and analysis**

Two reviewers (E.R.J.J. and G.A.F.D.) independently evaluated the list of titles and abstracts from each database. If at least one reviewer considered one study eligible, the full text was obtained for a complete assessment. Then, both reviewers independently assessed the full text of selected studies to verify if they met the criteria for inclusion or exclusion. Both reviewers independently extracted data from the published studies using standard data extraction forms adapted from the Cochrane Collaboration[10]. Aspects regarding the study population, intervention, outcome measures, and outcomes were retrieved. All studies selected from the databases were exported in an appropriate file and added to the Rayyan Software[12] for selection and data extraction independently by the two reviewers of the study.

**Methodological quality**

The quality of studies included in this systematic review was scored by two reviewers using the PEDro scale[13]. A third reviewer resolved any disagreements in the rating of the studies.

**Statistical assessment**

Pooled-effect estimates were obtained by comparing each group's mean change from baseline to endpoint. Thus, the outcomes' changes [post (-) pre-intervention] were extracted from each study and expressed as mean ± standard deviation. Within-group MD was calculated as the pretest–post-test change, divided by the pooled pretest standard deviation (SD). When studies presented data as mean ± standard error of the mean (SEM), SEM was converted to SD[14]. Conversion of nonparametric data to means and SD was based on recently established methods[15]. When the SD of change was unavailable, we used the confidence interval (CI) to convert it into SD, using the method described by Higgins et al[10]. When required outcome data were not available in the full text, the data were presented graphically, and an attempt was made to digitize the graph[16].

The SMDs of 0.2, 0.5, and 0.8 were considered to be small, moderate, and large, respectively[10]. An $\alpha$ value of 0.05 was considered significant. Calculations were done using a random-effects model. Statistical heterogeneity of the treatment effect among studies was assessed using Cochran's Q test and the $I^2$ inconsistency test statistic.

In this study, were adopted the values and interpretations 0% to 40% (might not be important); 30% to 60% (may represent moderate heterogeneity); 50% to 90% (may represent substantial heterogeneity); 75% to 100% (considerable heterogeneity)[10]. All analyses were conducted using Review Manager Version 5.4 (Cochrane Collaboration)[16].

**Certainty of evidence**

Certainty of evidence was assessed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach. Quantitative data from Cochrane's review manager was imported into GRADEpro GDT 2015 to create a "Summary of findings table" (SoF). The assessment involved five items: risk of bias, imprecision, inconsistency, indirectness, and publication bias. The certainty of evidence was downgraded by one level for risk of bias when more than a quarter of the studies included in the meta-analysis were considered at high risk of bias. Imprecision was mainly evaluated through visual analysis of the confidence intervals. When necessary, imprecision was evaluated by absolute risk analysis, number needed to treat, or optimal information size calculation. Continuous outcomes precision was parameterized based on clinical significance for the mean or standardized mean difference. Results were considered inconsistent if there was clinical or statistical heterogeneity (i.e., I2 > 40%) or no overlapping confidence intervals. When possible, publication bias was assessed by visually examining funnel plots (scatterplots of the effect size from individual studies against its standard error) for meta-analysis with at least ten trials[10,17]. Downgrade reasons were noted and attached to the SoF table.

## RESULTS

**Description of selected studies**

The initial search identified 645 abstracts, of which 69 were potentially relevant. Finally, six studies[18-23] met the eligibility criteria. The PRISMA flow diagram of studies is shown in Figure 1. All studies were scored using the PEDro scale. PEDro scores are presented individually in Table 1.

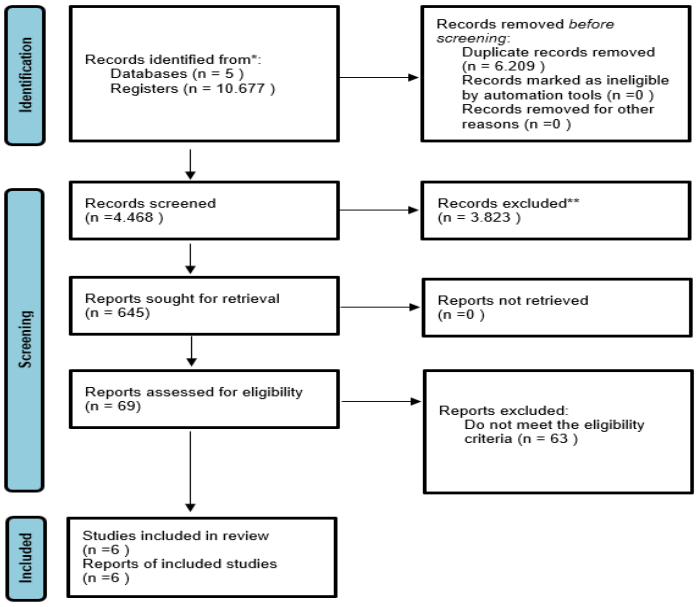


**Figure 1.** The PRISMA flow diagram

**Table 1.** Study quality on the PEDro scale.

| Study | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kuntz et al., 2018 | ✓ | ✓ | ✓ | ✓ | | | ✓ | ✓ | | ✓ | ✓ | 7 |
| Çolak et al., 2017 | ✓ | ✓ | ✓ | ✓ | | | | | ✓ | ✓ | ✓ | 6 |
| Allen et al., 2016 | ✓ | ✓ | ✓ | ✓ | | | ✓ | | ✓ | ✓ | ✓ | 7 |
| Jessep et al., 2009 | ✓ | ✓ | ✓ | ✓ | | | | ✓ | ✓ | ✓ | ✓ | 7 |
| McCarthy et al., 2004 | ✓ | ✓ | | ✓ | | | ✓ | ✓ | | ✓ | ✓ | 6 |
| Fransen et al., 2001 | ✓ | ✓ | ✓ | ✓ | | | | ✓ | ✓ | ✓ | ✓ | 7 |

Note: 1: eligibility criteria and source of participants; 2: random allocation; 3: concealed allocation; 4: baseline comparability; 5: blinded participants; 6: blinded therapists;7: blind assessors; 8: adequate follow-up; 9: intention-to-treat analysis; 10: between-group comparisons; 11: point estimates and variability. *Item 1 does not contribute to the total score

**Study Characteristics**

The number of participants with knee OA in RCTs included in this systematic review ranged from 30 to 320. Most of the included studies adequately reported the exercise protocol. Sample size, outcomes, and results of included studies are summarized in Table 2.

**Table 2.** Characteristics of included studies

| Study | Sample size | Sex/Age (y) | BMI | Outcomes | Key Findings | Dropouts % |
|---|---|---|---|---|---|---|
| Kuntz et al., 2018 | 31 (30) | - /66.7 | 30.4 | KOOS, ICOAP, LEFS, 6MWT, 40mW, 30Scs, TUG, Stair ascent, Muscle strength | There were no significant between-group differences for the evaluated outcomes. | 1 (3,3)% |
| Çolak et al., 2017 | 78 (56) | M (17) F (39)/ 59.5 | 30.9 | VAS, Muscle strength, 6MWT, IPAQ, Balance, | There were no significant between-group differences for the evaluated outcomes. | 22 (22,6%) |
| Allen et al., 2016 | 320 (260) | M (281) F (39) / 60 | 33.4 | WOMAC, SPPB | There were no significant between-group differences for the evaluated outcomes. | 60 (18.7%) |
| Jessep et al., 2009 | 64 (48) | M (4) F (44) / 66.5 | 29.5 | WOMAC, Aggregated functional performance time (AFPT) | There were no significant between-group differences for the evaluated outcomes. | 16 (25%) |
| McCarthy et al., 2004 | 214 (151) | - / 64.7 | 29.7 | ALF score, VAS, WOMAC | Group-based exercises demonstrated significantly more significant improvement in locomotor function (-3.7 seconds; 95% C.I. - 4.9 to - 2.5) and a decrease in walking pain | 63 (30%) |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | (- 15 mm; 95% C.I. - 20 to - 11) in relation to the group individualized exercise. | |
| Fransen et al., 2001 | 126 (107) | M (34) F (73) / 66.6 | 29.4 | WOMAC, SF-36 | There were no significant between-group differences for the evaluated outcomes. | 4 (3,2%) |

**Note:** M: Male; F: female; WOMAC: Western Ontario and McMaster Universities Arthritis Index, SF-36: Medical Outcomes Study Short Form; ALF: Aggregate locomotor function; VAS: visual analog scale; 6MWT: Six-Minute Walk Test; AFPT: Aggregated functional performance time; SPPB: Short Physical Performance Battery; IPAQ: Physical Activity Questionnaire; KOOS: Knee Injury and Osteoarthritis Outcome Score; ICOAP: Measure of Intermittent and Constant Osteoarthritis Pain; LEFS: Self-reported physical function; 40mW: 40-meter walk; 30s CS: 30-second chair stand; TUG: timed up and go.

**Effects of group-based versus individual exercise programs**

***Pain intensity***

Two RCTs assessed pain intensity using the Visual Analogue Scale (VAS, 0-100mm) as an outcome. The total number of people with knee OA in the group-based physical exercise was 137, whereas 109 patients were included in the individual exercise group. The meta-analyses showed (Figure 2a) that group-based exercise reduced pain intensity by MD -17.23 mm (95% CI: -22.15 to -12.31, I2 = 0%, n = 246 participants, with low-certainty evidence) compared to the individual exercise group.

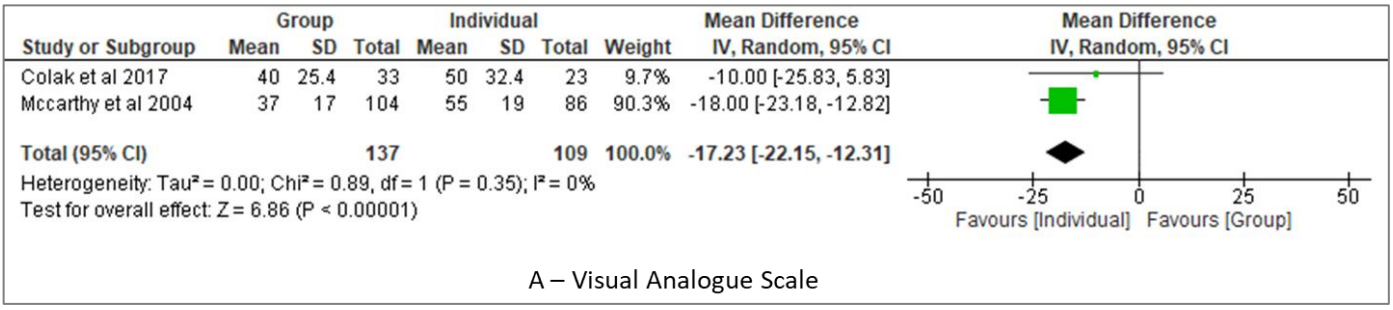


**Figure 2a.** Change in pain, Group versus individual exercises

**The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)**

***Pain subscale***

Four RCTs assessed the pain domain by WOMAC as an outcome. The total number of participants with knee OA in the group-based exercise was 316, whereas 313 patients were included in the individual exercise group. The meta-analyses showed (Figure 2b) that group-based exercise reduced pain intensity by MD -0.54 (95% CI: -1.0 to -0.08, I2=0%, n = 629 participants, with moderate-certainty evidence) compared to the individual exercise group.

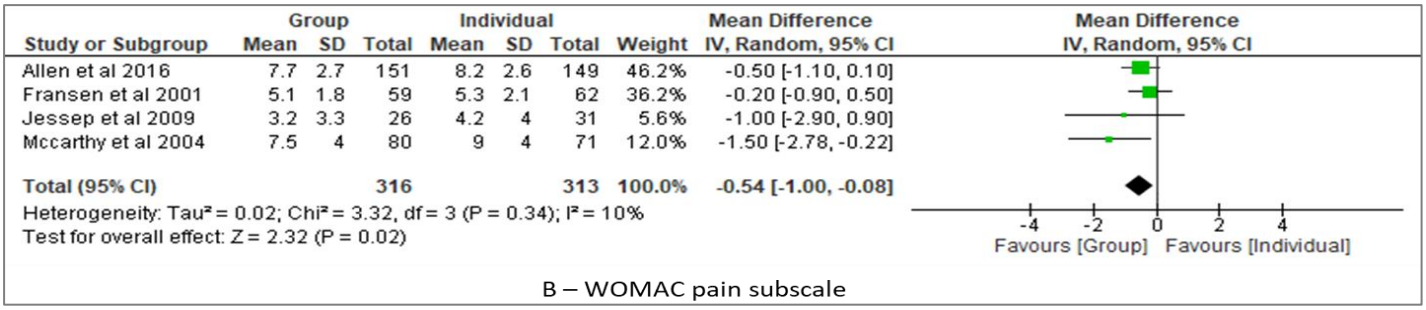


**Figure 2b.** Change in pain, Group versus individual exercises

***Function subscale***

Four RCTs assessed the function domain by WOMAC as an outcome. The total number of participants with knee OA in the group-based exercise was 316, whereas 313 patients were included in the individual exercise group. The meta-analyses showed (Figure 3a) that group exercise reduced the WOMAC function subscale by MD -2.09 (95% CI: -4.09 to -0.08, I2 = 0%, n = 629 participants, with moderate-certainty evidence) compared to the individual exercise group. The characteristics of the intervention programs are in Table 3.

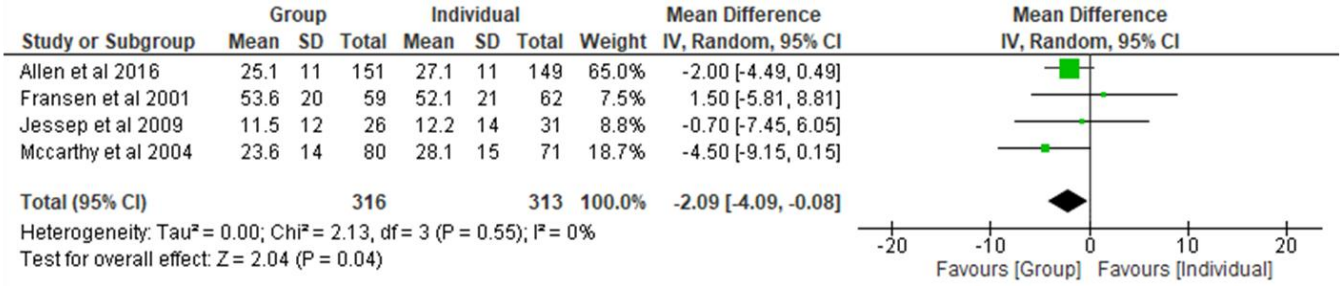


**Figure 3a.** Change in WOMAC function subscale

**Table 3.** The characteristics of exercises included

| Study | Group-based (GB)/ Individualized exercise(IE) | Exercises | Frequency (x per Wk/Wk) | Follow up (mth) |
|---|---|---|---|---|
| Kuntz et al., 2018 | GB (n=10)<br>IE (n= 11) | GB: by a certified, trained yoga instructor. It consisted of alignment-based postures that activate the lower limb musculature. The selected weight-bearing, static poses were performed barefoot and included squats and lunges with varying foot, trunk, and arm positioning. Careful attention was given to the ideal alignment of the leg throughout the exercises.<br>IE: knee strengthening, aerobic warm-up, balance exercises, and stretching.<br>Strengthening of shoulder and elbow flexors at 15 ° / s and wrist extensors at 60 °/s. | 1 / 12 | 4 |
| Çolak et al.,, 2017 | GB (n= 33)<br>IE (n= 23) | GB: Quadriceps muscle isometric contraction in sitting position, Hamstring muscle isometric contraction in sitting position, Hip adductor muscle isometric contraction in sitting position, Straight leg raise 4 way in lying position, Knee extension in sitting position Sit to stand exercise, Stand on one leg, Tandem walk, Walking with dorsiflexed and plantarflexed ankle.<br>IE: Quadriceps muscle isometric contraction in sitting position, hamstring muscle isometric contraction in sitting position, Hip adductor muscle isometric contraction in sitting position, Straight leg raise 4 way in lying position, Knee extension in sitting position, Sit to stand exercise, Stand on one leg, Tandem walk, Walking with dorsiflexed and plantarflexed ankle. | 3/6 | 1,5 |

| | | | | |
|---|---|---|---|---|
| Allen et al., 2016 | GB (n=159<br>IE (n =161) | GB: Core exercises, 4 stretching exercises (quadriceps muscle stretch, calf stretch, hamstring muscle stretch, and lower back and hip stretch) and 6 strengthening exercises (mini-squat, single-leg stand, chair stand, heel raises, hip abduction, and step-ups), based on an overall approach to enhancing lower extremity strength and flexibility<br>IE: Core exercises, 4 stretching exercises (quadriceps muscle stretch, calf stretch, hamstring muscle stretch, and lower back and hip stretch) and 6 strengthening exercises (mini-squat, single-leg stand, chair stand, heel raises, hip abduction, and step-ups), based on an overall approach to enhancing lower extremity strength and flexibility | 3/12 | 6 |
| Jessep et al., 2009 | GB (n= 60)<br>IE (n= 36) | GB: ESCAPE-knee pain (circuit of up to 10 exercises tailored to each participant's ability)<br>IE: The discretion of the treating physical therapist | 2/5 | 12 |
| McCarthy et al, 2004 | GB (n= 80)<br>IE (n= 71) | GB: Progressive resistance training, accelerated walking and stretching and balance exercises.<br>IE: Progressive resistance training, accelerated walking and stretching and balance exercises. | 2/8 | 12 |
| Fransen et al., 2001 | GB (n=36)<br>IE (n=39) | GB: Stretches, strengthening, weight-bearing eccentric, patella taping and Home program<br>IE: The discretion of the treating physical therapist. | 2/8 | 4 |

**Knee muscle strength**

***Knee extensors***

Three RCTs assessed knee extensor muscle strength as an outcome. The total number of participants with knee OA in the group exercise was 81, whereas 73 patients were included in the individual exercise group. The meta-analyses showed (Figure 3b) no significant between-group difference regarding the strength of the knee extensor muscles (SMD 0.4, 95% CI: -0.06 to 0.86, I2 = 44%, n = 154 participants, with very low-certainty evidence).

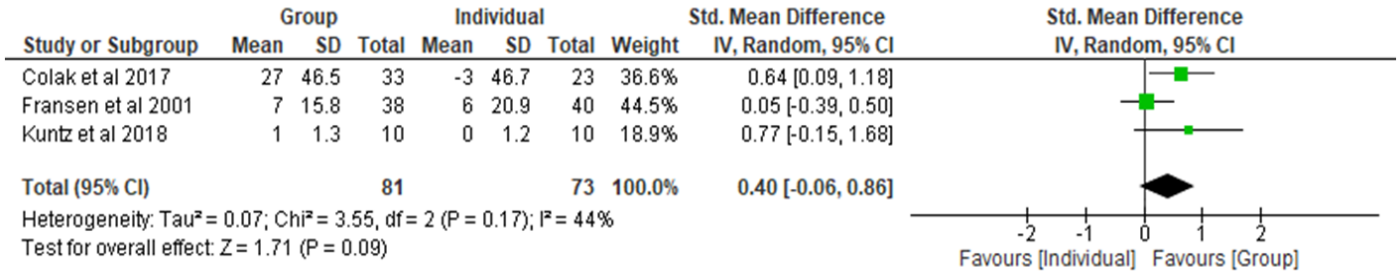


**Figure 3b.** Change in muscle strength versus individual exercises – Knee extensors

***Knee flexors***

Three RCTs assessed the strength of the knee flexor muscles as an outcome. The total number of participants with knee OA in the group-based exercise was 81, whereas 73 patients were included in the individual exercise group. The meta-analyses showed (Figure 3c) no significant between-group difference regarding the strength of the knee flexor muscles (SMD: -0.1, 95% CI: -0.75 to 0.53, I2: 70%, n = 154 participants, with very low-certainty evidence).

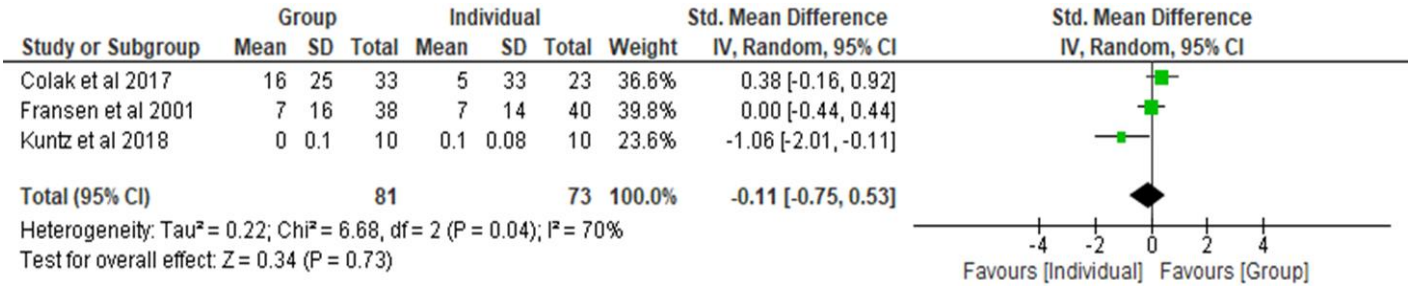


**Figure 3b.** Change in muscle strength versus individual exercises – Knee flexors

***Exercise tolerance***

Three RCTs assessed exercise tolerance to the six-minute walking test as an outcome. The total number of participants in the group-based exercise was 81, whereas 73 participants were included in the individual exercise group. The meta-analyses showed no significant between-group difference regarding exercise tolerance (SMD: -0.1, 95% CI: -0.75 to 0.53, $I^2$ = 70%, n = 154 participants, with very low-certainty evidence).

***Grade***

The certainty of evidence according to the GRADE system is presented in Figure 4.

**Figure 4.** Summary of findings

| **Group compared to Individual exercises for [Knee OA]** | | | | | | |
|---|---|---|---|---|---|---|
| Patient or population: [Knee OA]<br>Setting: Rehabilitation<br>Intervention: Group<br>Comparison: Individual | | | | | | |
| Outcomes | Anticipated absolute effects* (95% CI) | | Relative effect (95% CI) | № of participants (studies) | Certainty of the evidence (GRADE) | Comments |
| | Risk with Individual | Risk with Group | | | | |
| WOMAC pain | | MD **0.54 lower** (1 lower to 0.08 lower) | - | 629 (4 RCTs) | ⊕⊕⊕◯ Moderate[a] | |
| WOMAC function | | MD **2.09 lower** (4.09 lower to 0.08 lower) | - | 629 (4 RCTs) | ⊕⊕⊕◯ Moderate[a] | |
| 6WMT | | MD **1.34 lower** (35.46 lower to 32.77 higher) | - | 376 (3 RCTs) | ⊕◯◯◯ Very low[a,b,c] | |
| VAS | | MD **17.23 lower** (22.15 lower to 12.31 lower) | - | 246 (2 RCTs) | ⊕⊕◯◯ Low[a,c] | |
| Knee extensors | - | SMD **0.4 higher** (0.06 lower to 0.86 higher) | - | 154 (3 RCTs) | ⊕◯◯◯ Very low[a,b,c] | |
| Knee flexors | - | SMD **0.11 lower** (0.75 lower to 0.53 higher) | - | 154 (3 RCTs) | ⊕◯◯◯ Very low[a,b,c] | |

| |
|---|
| *__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).<br>**CI:** confidence interval; **MD:** mean difference; **SMD:** standardised mean difference |
| **GRADE Working Group grades of evidence**<br>**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.<br>**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.<br>**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.<br>**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect. |

## DISCUSSION

The main results of this study indicate that group-based exercise reduced pain intensity and disability measured by WOMAC compared with individual exercise programs in people with knee OA. Also, group-based and individual exercise programs effectively increased muscle strength and improved the 6-minute walk distance. In the studies included in this systematic review, the group exercise program ranged from 5 to 12 weeks, with a frequency of 2 to 3 times per week, totaling 10 to 36 sessions. According to Juhl et al.[24], optimal exercise programs for people with knee OA should be supervised, carried out three times weekly, and comprise at least 12 sessions; furthermore, they should have one aim and focus on improving lower extremity performance, muscle strength, and exercise tolerance. Iversen[25] summarized exercise studies for hip and knee OA and highlighted issues that influence the design, interpretation, and aggregation of results and how these factors impact data translation into clinical practice. From the data, it is unclear which intensity, frequency, mode, and duration are best for patients with hip and knee OA. The author suggests a strategy to assess the effectiveness of exercise doses. Multiply the total minutes of exercise per week by the duration of the program, stratify studies by total exercise dose, and examine the effect sizes of specific outcomes[25]. Due to the small number of included studies, we could not perform this dose analysis.

The MD in pain was -17.2 mm, favoring group-based physical exercise programs. Considering pain intensity for people with knee OA, the minimally clinically important difference (MCID) on a 0-100 VAS should at least be 16.2. In the WOMAC function subscale, the MCID should be at least 11.3[26]. The MD in the WOMAC function subscale was - 2.1, favoring group exercises. Thus, despite the clinically significant improvement in the pain intensity outcome, the improvement in function assessed by WOMAC cannot be considered clinically meaningful. Despite the benefits identified in this study regarding the investigated exercised modalities, the certainty of evidence for the analyzed outcomes was moderate to low due to the studies presenting moderate to low methodological quality and the inherent inconsistency and imprecision of group-level meta-analysis. Most RCTs failed to report the method for allocation concealment and Intention-to-treat analyses. Moreover, a high statistical significance heterogeneity was identified between the included studies after meta-analysis.

The result of this systematic review with metanalysis is limited. However, to instill confidence in the validity of our findings, we have taken rigorous steps to minimize the biases involved in this systematic review. These include the use of criteria for methodological quality, the presence of two independent reviewers, a wide search in multiple databases without language or time restrictions, and specific tools for the analyses.

## CONCLUSION

Our systematic review showed that group-based physical exercise reduced pain intensity and disability measured by WOMAC compared to individual exercise programs in people with knee OA. Furthermore, group-based and individual physical exercise programs effectively increased muscle strength and improved the 6-minute walk distance.

**Author Contributions:** Conception and design of the study: E.R.J.J., C.L.L., F.T.-S., T.F.A.S.; Data acquisition: E.R.J.J., C.L.L., G.A.F.D; Data analysis and interpretation: E.R.J.J., C.L.L., G.A.F.D, M.G.N., D.C.M.M., F. D. A. A., F.T.-S, T.F.A.S.; Preparation of the manuscript: E.R.J.J., C.L.L., G.A.F.D, M.G.N., D.C.M.M., F. D. A. A., F.T.-S, T.F.A.S.; Intellectual review of the manuscript: E.R.J.J., C.L.L., G.A.F.D, M.G.N., D.C.M.M., F. D. A. A., F.T.-S, T.F.A.S.; Final approval of the manuscript: E.R.J.J., C.L.L., G.A.F.D, M.G.N., D.C.M.M., F. D. A. A., F.T.-S, T.F.A.S.

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**Conflict of interest:** The authors declare they do not have direct or indirect benefits that constitute professional or financial conflicts of interest that may influence the study's results or scientific disclosure.

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