Author/s:
Marriott, KA;Hall, M;Maciukiewicz, JM;Almaw, RD;Wiebenga, EG;Ivanochko, NK;Rinaldi, D;Tung, EV;Bennell, KL;Maly, MR

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Are the Effects of Resistance Exercise on Pain and Function in Knee and Hip Osteoarthritis Dependent on Exercise Volume, Duration, and Adherence? A Systematic Review and Meta-Analysis

Kendal A. Marriott,[1] Michelle Hall,[2] Jacquelyn M. Maciukiewicz,[1] Rachel D. Almaw,[1] Emily G. Wiebenga,[1] Natasha K. Ivanochko,[1] Daniel Rinaldi,[1] Emma V. Tung,[1] Kim L. Bennell,[2] and Monica R. Maly[1]

Objective. The purpose of this study was to determine dose parameters for resistance exercise associated with improvements in pain and physical function in knee and hip osteoarthritis (OA) and whether these improvements were related to adherence.

Methods. We searched six databases, from inception to January 28, 2023, for randomized controlled trials comparing land-based, resistance exercise–only interventions with no intervention, or any other intervention. There were four subgroups of intervention duration: 0 to <3 months, 3 to 6 months, >6 to <12 months, ≥12 months. The between-group effect was calculated for immediate postintervention pain and physical function (activities of daily living [ADL] and sports/recreation [SPORT]).

Results. For both knee and hip, data from 280 studies showed moderate benefit for pain, physical function ADL, and physical function SPORT in favor of interventions 3 to 6 months. For the knee, there was also a moderate benefit for physical function ADL in favor of interventions >6 to <12 months. From 151 knee and hip studies that provided total exercise volume data (frequency, time, duration), there was no association between volume with the effect size for pain and physical function. A total of 74 studies (69 knee, 5 hip) reported usable adherence data. There was no association between adherence with the effect size for pain and physical function.

Conclusion. In knee and hip OA, resistance exercise interventions 3 to 6 months (and for the knee >6 to <12 months) duration improve pain and physical function. Improvements do not depend on exercise volume or adherence, suggesting exercise does not require rigid adherence to a specific dose.

INTRODUCTION

Exercise is endorsed for the management of knee and hip osteoarthritis (OA) across international clinical guidelines.[1,2] Improvements in OA symptoms with exercise are comparable to pain medications[3] but with additional benefit to overall health[4] and without unwanted side effects that often accompany medications.[5] However, the clinical relevance of improvements in pain and function with exercise in people with knee and/or hip OA has recently been questioned.[6–8] Factors that likely contribute to the exercise response include the affected joint, parameters of prescription (eg, type, duration, volume) and adherence.[9–13] Due to the variable response to exercise, there is a substantial gap in guiding exercise for knee and/or hip OA.

Indirect evidence from systematic reviews on exercise for knee OA[10,14,15] and hip OA[10,11,14] suggests that the benefits may be lower in hip OA than knee OA. Thus, the effects of exercise should be assessed according to the affected joint. Previous

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[1]Kendal A. Marriott, PT, PhD, Jacquelyn M. Maciukiewicz, PhD, Rachel D. Almaw, BSc, Emily G. Wiebenga, BSc, Natasha K. Ivanochko, MSc, Daniel Rinaldi, BSc, Emma V. Tung, MSc, Monica R. Maly, PT, PhD: The University of Waterloo, Waterloo, Ontario, Canada; [2]Michelle Hall, PhD, Kim L. Bennell, PhD: The University of Melbourne, Melbourne, Victoria, Australia.

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Address correspondence via email to Monica R. Maly, PT, PhD, at mrmaly@uwaterloo.ca.

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SIGNIFICANCE & INNOVATIONS

- Improvements in pain and physical function in knee and hip osteoarthritis (OA) do not depend on exercise volume or participant adherence.
- Resistance exercise interventions 3 to 6 months duration improve pain and physical function in both knee and hip OA.
- These findings highlight the flexibility available for clinicians in the prescription of resistance exercise for knee and hip OA without compromising improvements in pain and physical function.

systematic reviews[9,10,13–16] investigating the effects of exercise in knee and hip OA evaluated a combination of exercise types, such as resistance, flexibility, and cardiovascular exercise. However, the response to exercise might differ according to type of exercise,[10] introducing heterogeneity in both the delivered exercise intervention and outcomes. Furthermore, muscle weakness is common with knee and hip OA[17–20] and associated with progressive structural and symptomatic changes,[18,21–23] which likely explains why resistance exercise is most frequently studied.[10,24] Taken together, these observations support the investigation of resistance exercise alone on pain and physical function specific to the affected joint.

Exercise dosage is determined by frequency, volume, time, intensity, and duration of the program.[25] Some evidence from a systematic review on resistance exercise for knee OA suggests an exercise program 8 to 12 weeks duration confers the largest benefits in pain and function compared to interventions that are shorter or longer in duration.[24] Additional evidence from systematic reviews proposes that exercise programs that comply with exercise dosage according to the American College of Sports Medicine [ACSM] recommendations (150 minutes/week moderate aerobic exercise, 2–4 sets of 8–12 repetitions of 60%–70% one repetition maximum resistance exercise) have benefits in hip OA[13] but not in knee OA[15] when compared to trials with questionable compliance to dosage recommendations. These reviews further support the contention that the effects of exercise should be assessed according to the affected joint. It remains uncertain whether resistance exercise programs that comply with ACSM guidelines result in greater benefits, because these previous reviews evaluate programs not isolated to resistance exercise. Moreover, insights into the individual components of dosage may help optimize the benefits of resistance exercise.

The effects of resistance exercise on knee and hip OA pain and physical function are further complicated by adherence to exercise. It is a widely held belief that poor adherence is a barrier to achieving and maintaining the benefits of exercise.[12,26] However, the evidence is conflicting[12,26,27] and predominately in knee OA. The relationship between adherence and clinical outcomes requires further exploration to inform recommendations that promote clinically meaningful improvements. Therefore, this systematic review and meta-analysis aimed to examine dose parameters for land-based, resistance exercise interventions that are associated with improvements in pain and physical function in knee and hip OA. We also investigated whether these improvements related to participant adherence to resistance exercise.

METHODS

Search strategy. The following electronic bibliographic databases were systematically searched from dates of inception to July 28, 2020: PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Excerpta Medica Database (EMBASE), MEDLINE Ovid, and Scopus. This search was updated to January 28, 2023. Results were limited to randomized controlled trials (RCTs) on humans published in the English language. An example of the PubMed search is provided in Table 1. Title, abstract, and full-text screening was performed independently by multiple (any 2 of 6) reviewers. Six reviewers (KAM, EGW, DR, EVT, NKI, and JMM) conducted title, abstract, and full-text screening. A seventh reviewer (MRM) was involved for discrepancies between the two assigned reviewers. Data extraction was completed independently in duplicate (JMM, RDA, and KAM). The protocol for this systematic review and meta-analysis was prospectively registered (PROSPERO CRD42020190217).

Inclusion criteria. RCTs had to fulfill the following criteria to be included in the meta-analysis: adults meeting the American College of Rheumatology diagnostic criteria for knee or hip OA (clinical, radiographic, or laboratory) or who self-report knee or hip OA;[28] at least one study arm is a land-based, resistance exercise intervention alone; and report at least one of the following pain and/or physical function outcomes: visual analog scale, numeric pain rating scale, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Knee Injury and Osteoarthritis Outcome Scale (KOOS), or Hip Disability and Osteoarthritis Outcome Score (HOOS).

Exclusion criteria. RCTs were excluded according to the following criteria: not knee or hip joint, no full text available (eg, conference abstract, study proposal or protocol); children and adolescents (ie, <18 years old); no relevant pain or function outcomes (previously defined).

Dependent variables. The primary dependent outcomes were the change in patient-reported knee or hip pain and physical function. Pain was obtained from one of the following: visual analog scale, numeric pain rating scale, pain subscale of the WOMAC, or pain subscale of the KOOS or HOOS. Physical function was obtained from one of the following: function subscale of

Table 1. Example of search strategy used for PubMed database

Osteoarthritis	Pain, function	Strengthening exercise
osteoarthr*[tiab]	pain[tiab]	exercis*[tiab]
osteoarthritis[mh]	pain[mh:noexp]	exercise[mh:noexp]
osteoarthritis, knee[mh]	pain management[mh]	exercise therapy[mh:noexp]
osteoarthritis, hip[mh]	musculoskeletal pain[mh]	((resistance OR strength* OR isometric OR isokinetic OR isotonic OR weight OR static OR plyometric) AND train*)
oa[tiab]	pain measurement[mh]	(exercis*[tiab] AND therapy[tiab])
arthr*[tiab]	pain, procedural[mh]	weightlifting[tiab]
arthritis[mh:noexp]	arthralgia[mh]	weight lifting[tiab]
	((knee[tiab] OR hip[tiab] OR physical[tiab]) AND function[tiab])	resistance machine*[tiab]
	recovery of function[mh]	resistance training[mh]
	range of motion, articular[mh]	muscle strength[mh]
	muscle strength[mh]	muscle strength dynamometer[mh]
	torque[mh]	circuit-based exercise[mh]
	muscle contraction[mh]	plyometric exercise[mh]
	visual analog scale[tiab]	exercise movement techniques[mh]
	visual analogue scale[tiab]	
	visual analog scale[mh]	
	vas[tiab]	
	numeric pain rating scale[tiab]	
	nprs[tiab]	
	knee injury osteoarthritis outcome score[tiab]	
	koos[tiab]	
	osteoarthritis outcome score[tiab]	
	hip disability osteoarthritis outcome score[tiab]	
	hoos[tiab]	
	western ontario mcmaster universities osteoarthritis index[tiab]	
	womac[tiab]	
Filters		
(randomized controlled trial[ptyp] OR randomized[tw] OR randomised[tw] OR random[tw] OR placebo[tw] OR double-blind[tw]) NOT (animals[mh] NOT human[mh])		
NOT (review[ptyp] OR systematic review[ptyp] OR meta-analysis[ptyp] OR clinical trial protocol[ptyp] OR comment[ptyp] OR patient education handout[ptyp] OR editorial[ptyp] OR newspaper article[ptyp] OR (following[ti] AND arthroplasty[ti]) OR (after[ti] AND arthroplasty[ti]) OR (following[ti] AND replacement[ti]) OR (after[ti] AND replacement[ti]))		
english[la]		

the WOMAC, activities of daily living function subscale of the KOOS or HOOS, or sport and recreation function subscale of the KOOS or HOOS. Because the KOOS and HOOS both contain two different measures of physical function (activities of daily living [ADL] function and sport and recreation [SPORT] function), these subscales were analyzed separately. Therefore, there was one pain-dependent variable and two function-dependent variables (physical function ADL and physical function SPORT). For all dependent variables, the immediate postintervention outcomes were extracted.

If more than one pain or physical function outcome was evaluated in a study, only one pain and one physical function outcome was analyzed. The single outcome was selected according to the following predefined hierarchy.[29] (i) Visual analog scale, (ii) numeric pain rating scale, (iii) pain and function subscales of the WOMAC, (iv) pain and activities of daily living function and sport and recreation function subscales of the KOOS or HOOS.

Independent variables. *Exercise dose.* Four parameters were extracted: intensity, frequency, time, and duration. Three domains of exercise intensity were extracted: number of repetitions per set per exercise, number of sets per exercise, and number of exercises. However, exercise intensity was not evaluated due to inconsistency in reporting. Exercise frequency was defined as the number of times per week participants exercised (sessions/week). Exercise time was defined as the exercise session duration, including warm-up/cool-down (minutes/session). Intervention duration was defined as the total number of weeks over which the intervention occurred. Three of these parameters (frequency, time, duration) were multiplied to produce a total volume parameter. Intervention duration was categorized into four subgroups, according to the following timepoints: <3 months, 3 to 6 months, >6 to <12 months, and ≥12 months.

Participant adherence. Adherence data that were extracted included either the rate reported (percent) within the publication or the rate (percent) calculated by the current research team from two reported pieces of information—total number of exercise sessions prescribed and the average number of exercise sessions completed.

Multiarm studies. For studies with more than one comparator group, the comparator groups were combined into a

single control group. Therefore, the extracted data for the comparator groups were aggregated and compared to the extracted data for the experimental group.

Calculation of effect size and SD. A random effects model was used to pool the data. For all studies, the mean change score (mean postintervention score minus mean baseline score) and corresponding SD were extracted. If no change score was reported, the postintervention score and corresponding SD were extracted. The effect size (ES) for each dependent variable was calculated by using the standardized mean difference (SMD) and was interpreted consistent with published cut-off values: small (ES 0.2), moderate (ES 0.5) and large (ES 0.8).[30] If a study reported the within-group standard error or 95% confidence intervals (CIs) instead, the SD was calculated using the following formulas, respectively (https://training.cochrane.org/handbook/current/chapter-06):

$$SD = SE \times \sqrt{N}, \quad \text{(Equation 1)}$$

where *SE* is the standard error and *N* is the sample size;

$$SD = \sqrt{N \times \left(\frac{upper\ limit - lower\ limit}{2 \times tinv(probability, df)}\right)}, \quad \text{(Equation 2)}$$

where *N* is the sample size, *upper limit – lower limit* is the 95% CI, and *tinv(probability, df)* is the value from a t distribution, given 95% CI and N – 1.

Statistical analyses. Data analysis was completed using R (version 4.12). All analyses were completed separately for the knee and hip.

Intervention duration. One subgroup analysis was performed to determine the potential effects of exercise duration on pain and physical function. Intervention duration was categorized into four subgroups: <3 months, 3 to 6 months, >6 to <12 months, and ≥12 months.

Meta-Regression analyses. Two meta-regression analyses were performed for each dependent variable. The dependent variables were the ES for pain and physical function ADL or physical function SPORT. The baseline ES of the corresponding outcome was entered as a covariate for each analysis. For the first meta-regression, the independent variable was total volume (days × minutes × weeks). For the second meta-regression, the independent variable was participant adherence to exercise intervention (percent). Significance for meta-regressions was set at $P < 0.05$.

Heterogeneity. Heterogeneity between studies was evaluated using the I^2 statistic. An $I^2 < 25\%$, between 26% and 50%, and >51% was considered low, moderate, and high heterogeneity, respectively.[31]

Risk of bias and quality assessment. The Cochrane risk of bias assessment tool (version 2) was used to assess the risk of bias within each study. This assessment was performed independently by two reviewers (KAM, RDA). If scores did not match, a third reviewer (JMM) was involved to reach consensus.

Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) was used to synthesize the overall strength of the evidence, following direction from the GRADE Handbook.[32] The overall quality of evidence was categorized as "high," "moderate," "low," and "very low." Because all included studies were RCTs, evidence was initially considered "high," and evidence was downgraded to "moderate," "low," or "very low" depending on the number of concerns associated with risk of bias, inconsistency, indirectness, imprecision, and publication bias. Funnel plots and Egger's test were used to assess for publication bias. Four reviewers reached consensus on GRADE scores.

Consensus on Exercise Reporting Template (CERT) was used to evaluate the reporting of essential items required to replicate exercise programs.[33] One reviewer completed the CERT, which was subsequently verified by independent review. Discrepancies were resolved by a third reviewer.

RESULTS

Our search retrieved 13,489 citations (dates of inception to January 28, 2023), of which 280 studies were eligible and were included in the meta-analysis (Figure 1). During the title and abstract screening and full-text screening, the mean interrater reliability (Cohen's κ) between reviewer pairs was 0.83 and 0.69, respectively.

A total of 10,261 participants were allocated to exercise and 14,928 participants to control. Of the participants in exercise, 9,404 reported knee OA, and 462 reported hip OA; 76.6% were females; the mean age was 62.3 years, and the mean body mass index (BMI) was 28.7 kg/m^2. Of the controls, 13,732 reported knee OA, and 630 reported hip OA; 75.1% were females; the mean age was 62.1 years, and the mean BMI was 28.7 kg/m^2.

Intervention duration. *Knee.* The forest plots for the knee for pain, physical function ADL, and physical function SPORT are presented in Supplementary Figures 1, 2 and 3, respectively. In summary, the ES (95% CI) for each intervention duration (<3 months, 3–6 months, >6 to <12 months, and ≥12 months) for pain was –0.09 (–0.26 to 0.08; –0.38 (–0.56 to –0.21); –0.18 (–0.52 to 0.15); 0.12 (–0.05 to 0.30), respectively; for physical function ADL, ES (95% CI) was –0.24 (–0.62 to 0.15); –0.32 (–0.50 to –0.15); –0.30 (–0.56 to –0.05); 0.10 (–0.05 to 0.25), respectively; and for physical function SPORT, ES (95% CI) was –0.15 (–0.48 to 0.19); –0.33 (–0.52 to –0.14); –0.19 (–0.38 to 0.01); 0.06 (–0.11 to 0.23), respectively.

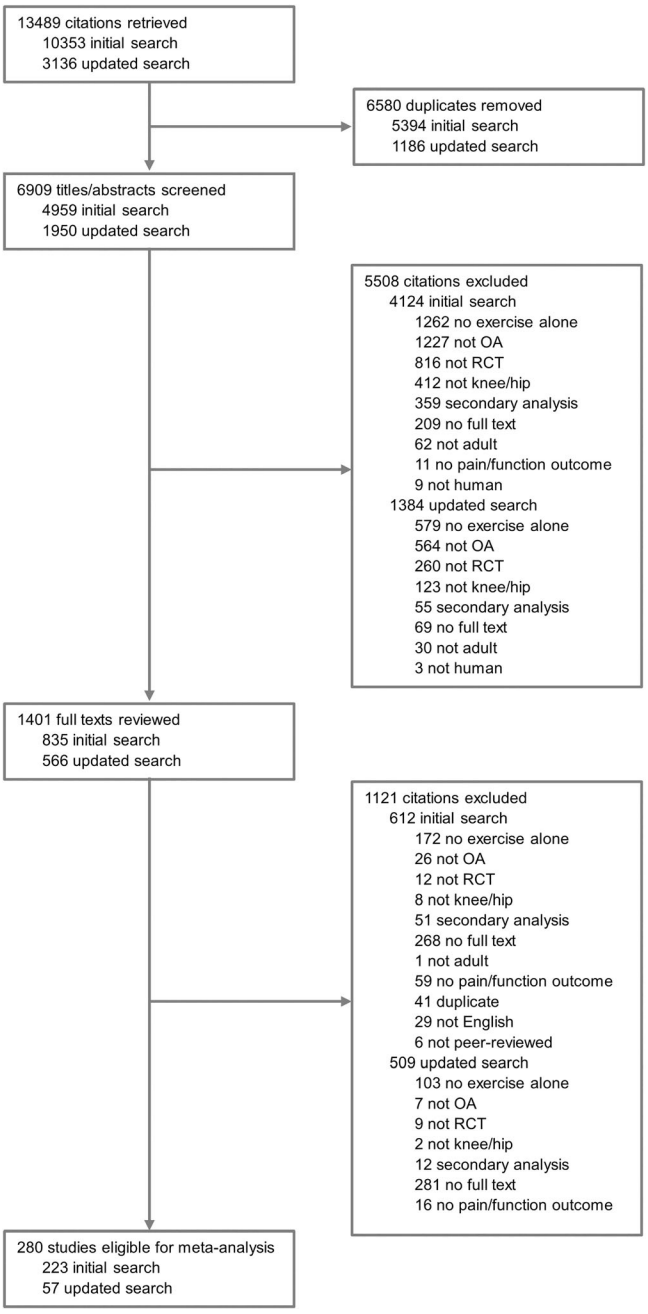

Figure 1. Flow diagram of study selection. OA, osteoarthritis; RCT, randomized controlled trial.

For pain, there was a moderate benefit favoring exercise for interventions 3 to 6 months duration (ES –0.38, 95% CI –0.56 to –0.21), and this benefit was significantly greater relative to interventions <3 months (β = –0.30, 95% CI –0.54 to –0.06; $P = 0.016$). There was no benefit for interventions <3 months, >6 to <12 months, or ≥12 months duration. For physical function ADL, there was a moderate benefit favoring exercise for interventions 3 to 6 months duration (ES –0.32, 95% CI –0.50 to –0.15) and interventions >6 to <12 months duration (ES –0.30, 95% CI –0.56 to –0.05), although neither benefit was significantly greater relative to <3 months ($P > 0.05$). There was no benefit for exercise interventions <3 months or ≥12 months duration. For physical function SPORT, there was a moderate benefit favoring exercise for interventions 3 to 6 months duration (ES –0.33, 95% CI –0.52 to –0.14), although this benefit was not significantly greater relative to <3 months ($P > 0.05$). There was no benefit for interventions <3 months, >6 to <12 months, or ≥12 months duration.

Hip. The forest plots for the hip for pain, physical function ADL, and physical function SPORT are presented in Supplementary Figures 4, 5 and 6, respectively. No studies reported exercise interventions that were >6 to <12 months or ≥12 months duration. In summary, the ES (95% CI) for each intervention duration (<3 months and 3 to 6 months) for pain was 0.17 (–0.37 to 0.71); –0.45 (–0.67 to –0.22), respectively; for physical function ADL, the ES (95% CI) was –0.33 (–0.83 to 0.17); –0.61 (–1.10 to –0.12), respectively; and for physical function SPORT, ES (95% CI) was –0.29 (–0.74 to 0.15); –0.61 (–1.10 to –0.12), respectively.

For pain, there was a moderate benefit favoring exercise interventions 3 to 6 months duration (ES –0.45, 95% CI –0.67 to –0.22), and this benefit was significantly greater relative to interventions <3 months (β = –0.62, 95% CI –1.20 to –0.03; $P = 0.039$). There was no benefit for interventions <3 months duration. For physical function ADL, there was a moderate benefit favoring exercise for interventions 3 to 6 months duration (ES –0.61, 95% CI –1.10 to –0.12), although this benefit was not significantly greater relative to <3 months ($P > 0.05$). There was no benefit for interventions <3 months duration. For physical function SPORT, there was a moderate benefit favoring exercise for exercise interventions 3 to 6 months duration (ES –0.61, 95% CI –1.10 to –0.12), although this benefit was not significantly greater relative to <3 months ($P > 0.05$). There was no benefit for exercise interventions <3 months duration.

Total volume. A total of 151 of 280 studies provided complete information related to total volume (frequency, time, duration); 153 of 280 studies provided complete information related to all three domains of exercise intensity (repetitions, sets, number of exercises), although these data were inconsistently reported and thus difficult to quantify. For the knee, there was no association between total volume and the ES for pain (β = 0.00, 95% CI –0.00 to 0.00; $P > 0.05$), physical function ADL (β = 0.00, 95% CI –0.00 to 0.00; $P > 0.01$), or physical function SPORT (β = 0.00, 95% CI –0.00 to 0.00; $P > 0.01$). For the hip, the association between total volume and the ES for pain (β = –0.00, 95% CI –0.00 to –0.00; $P < 0.01$) was negligible. There was no association between total volume and the ES for physical function ADL (β = –0.00, 95% CI – 0.00 to 0.00; $P > 0.05$) or physical function SPORT (β = –0.00, 95% CI – 0.00 to 0.00; $P > 0.05$).

Participant adherence. For the knee, 69 (26.8%) of the 257 studies on knee OA reported usable adherence data. There

Table 2. Summary of study quality using GRADE*

Outcome measure	SMD (95%CI)	I^2, %	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Other
Pain	−0.19 (−0.07 to −0.30)	93.39	RCT	Serious (−1)	Very serious (−2)	No	No	No	No plausible confounding (+1)
Physical function ADL	−0.25 (−0.08 to −0.43)	96.35	RCT	Serious (−1)	Very serious (−2)	No	No	No	No plausible confounding (+1)
Physical function SPORT	−0.23 (−0.06 to −0.40)	95.22	RCT	Serious (−1)	Very serious (−2)	No	No	No	No plausible confounding (+1)

* Physical function included both ADL function and SPORT function. ADL, activities of daily living; CI, confidence interval; GRADE, Grades of Recommendation, Assessment, Development and Evaluation; RCT, randomized controlled trial; SMD, standardized mean difference; SPORT, sport and recreation.

was no association between adherence and the ES for pain (β = 0.01, 95% CI −0.01 to 0.02; $P > 0.05$), physical function ADL (β = −0.01, 95% CI −0.03 to 0.01; $P > 0.05$), or physical function SPORT (β = −0.01, 95% CI −0.02 to 0.00; $P > 0.05$). For the hip, 5 (33.3%) of the 15 studies on hip OA reported usable adherence data. There was no association between adherence and the ES for pain (β = 0.15, 95% CI −0.10 to 0.40; $P > 0.05$). There were not enough studies to evaluate the association between adherence and the ES for physical function measures.

Cochrane risk of bias. A high risk of bias was related to lack of blinding for both participants (100% of studies) and individuals delivering interventions (99% of studies), which is relatively unavoidable in exercise studies. A high risk of bias was also related to outcome assessors being aware of the intervention received by participants (100% of studies). Because outcomes assessed were self-reported, the assessors were the participants. The lowest risk of bias was related to adequate randomization (73% of studies), lack of baseline differences between groups suggesting minimal problems with randomization (93% of studies), availability of data for all or nearly all participants (67% of studies), and analysis of data according to at least one element of the prespecified analysis plan (99%).

GRADE. Table 2 summarizes study quality. Because there was a high risk of bias related to (i) a lack of blinding for participants and individuals delivering interventions and (ii) outcome assessors being aware of the intervention received by participants, risk of bias was downgraded to "serious" (−1). Inconsistency was downgraded to "very serious" (−2) because of the variety of interventions included as a control group. Other was upgraded (+1) on the basis of no plausible confounding.

Funnel plots and CERT. Funnel plots for the knee and hip for all outcomes are presented in the Supplementary Figures 7 through 12. The mean CERT score was 10 (range 0–19) out of a maximum score of 19. Three of 280 studies adequately described all aspects of exercise interventions in accordance with CERT. Details of the standard of reporting for each of the 16 criteria is provided in Figure 2. We also repeated the analysis after dichotomizing by CERT score (low [0–9] versus high [10–19] CERT score). Results of this exploratory analysis were similar to the original analysis. Details are provided in Supplementary Table 1.

DISCUSSION

The current analysis of a large number of trials in knee and hip OA shows that the effect of land-based resistance exercise on pain and physical function varied based on affected joint and exercise duration. For both the knee and hip joints, based on moderate quality evidence, there was a moderate benefit observed for pain and physical function favoring exercise interventions three to six months duration. The magnitude of the SMDs are comparable to SMDs obtained from previous meta-analyses on different types of exercise for knee and hip OA.[10,13,15,16] These findings suggest that pain and physical

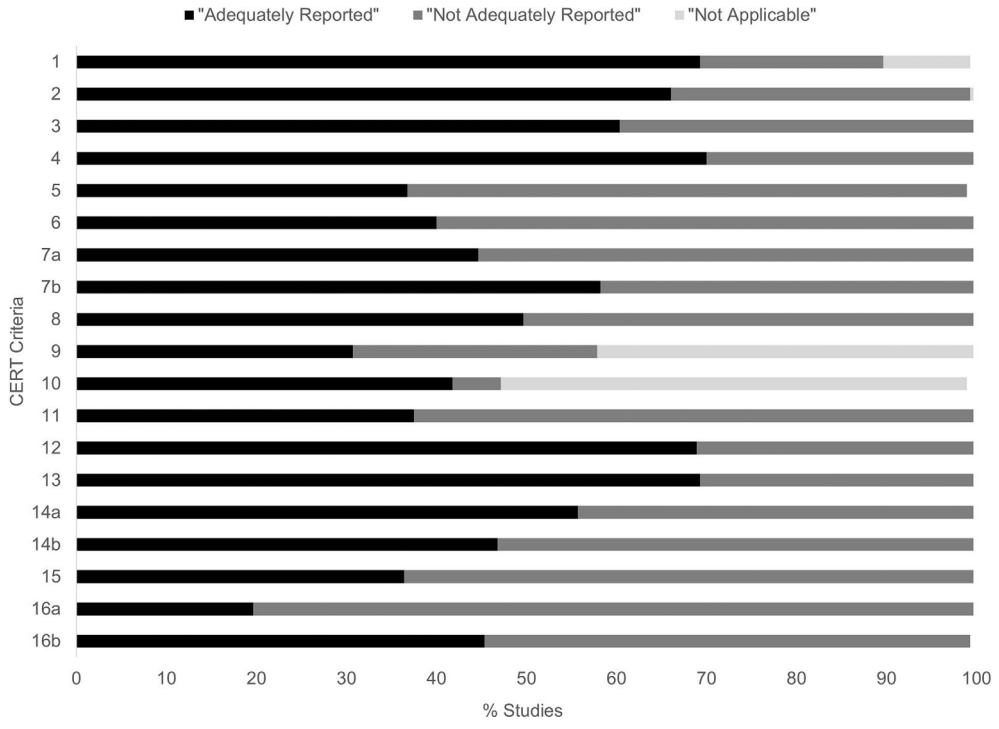

Figure 2. Quality of exercise intervention reporting assessed using the CERT. CERT, Consensus on Exercise Reporting Template.

function improvements for knee and hip OA from exercise are optimized by interventions that are three to six months duration and do not depend on the prescribed exercise volume or participant adherence. Clinicians can focus on strategies to engage individuals with knee and hip OA in at least some form of resistance exercise without a need to rigidly adhere to a certain volume to achieve exercise benefits over the required duration of three to six months.

For both knee and hip OA, benefits were greatest for exercise interventions three to six months duration rather than <3 months or ≥12 months duration. There is no clear consensus on the optimal duration of exercise interventions for improving pain and function in knee and hip OA; however, previous meta-analyses found greater improvements in pain and function with shorter interventions (an average of 27 weeks) compared to longer interventions (2 years)[24] or no difference between shorter (<12 sessions) and longer (>12 sessions) interventions.[13] OA resistance exercise interventions lasting ≥1 year did not confer a greater treatment effect in our meta-analysis, likely reflecting several considerations. First, relatively few studies implement exercise interventions longer than 12 months, limiting sample size. It is noteworthy that the changes in pain and physical function for these interventions favored neither the exercise nor control intervention. Second, the nature of the control interventions of these long duration studies included active treatments that minimized the difference between the intervention and control groups.[34,35] These control groups often provided diet with behavioral sessions,[36] another exercise,[37] or pharmacological intervention,[38] producing comparable improvements as exercise. Third, it is possible that there is a ceiling to the magnitude of improvement in pain and physical function, whereby further investment in resistance exercise provides diminishing returns. Clinical outcomes in OA are influenced by multiple factors, including pain sensitization, psychological distress, muscle strength, BMI, inflammation, disease severity, and comorbidities,[39] which may ultimately limit the maximum improvement in pain and function. If true, it remains essential for clinicians to view these longer duration interventions as a means to provide maintenance of pain and physical function improvements, rather than escalating performance. Exercise interventions lasting three to six months may provide an opportunity for participants to achieve the maximal positive benefits of exercise on pain and physical function for both knee and hip OA, and the large number of studies provide adequate power to detect such an effect.

For both knee and hip OA, there was no association between participant adherence and ES for pain or physical function. Participant adherence may decline over time in exercise trials[40] due to multiple factors, including participant characteristics,[27,40] intervention characteristics,[27,40] and symptom improvement,[12,27] although there is no clear consensus regarding the factors that may predict poor adherence.[27,40] Further complicating, it is difficult to assess the impact of poor adherence to a prescribed exercise dose on OA outcomes because fewer than half of exercise trials for musculoskeletal conditions measure adherence, and nearly 25% of these studies do not report exercise adherence results.[41] In the current analysis, the lack of relationship between outcomes with adherence for both knee and hip OA indicates that participant adherence has minimal effect on outcomes, regardless of the intervention duration.

Previous work, including a narrative review and systematic review of 12 studies on knee OA, suggested that there is no optimal exercise dose for improving pain and function in OA.[24,42] Findings from the current comprehensive systematic review and meta-analysis suggest total exercise volume is not related to improvements in pain in knee OA. Indeed, this finding appears consistent with recent publications questioning the efficacy of exercise trials in OA and, more specifically, the potentially greater influence of contextual factors (eg, placebo effects) on observed improvements after exercise trials over the specific effects of the exercise intervention.[6–8] Although a weak association of total exercise volume with improvements in pain may be present in hip OA, there were a limited number of studies, and only about 50% (152 of 280) provided adequate information to calculate total volume. Therefore, it is difficult to draw firm conclusions regarding the relationship. This finding is consistent with previous studies suggesting compliance with the ACSM exercise dosage recommendations may produce greater benefits for hip OA[13] but not knee OA.[15] Exercise intensity (load, repetitions, sets, number of exercises) was not included in the current calculation of exercise volume but may also impact exercise adaptations.[4,43,44] Findings regarding the effects of exercise intensity on pain and physical function in OA are uncertain,[34] and reporting of exercise intensity in trials is variable and relatively poor overall.[24] In the current study, only 153 of 280 (55%) studies provided complete information related to all three exercise intensity domains. Overall, the measure of total volume in the current study may not adequately capture the factors that ultimately impact pain and physical function. There are also a number of proposed mechanisms through which exercise may provide improvements in pain and physical function independent of total volume, including improvement in overall mental health, depressive symptoms and self-efficacy,[16,45] and mitigation of joint inflammation.[46] Future studies should ensure both exercise volume and exercise intensity are adequately reported. Additionally, trials presenting the number of repetitions and sets as a range and the lack of clarity of how these domains are modified at different intervals in a progressive program, make it difficult to accurately quantify exercise intensity. Therefore, it may be useful to standardize reporting of exercise dose as a "total dose" calculation that accounts for both exercise volume and exercise intensity and a description of how this total dose is progressed from beginning to end of the intervention period (eg, from one set of 8 repetitions to three sets of 10 repetitions). A standardized report of "exercise dose" would enable meaningful comparison of exercise interventions between studies.

There are limitations. Only self-reported pain and physical function were included. Due to the nature of exercise interventions, participants were not blinded to group allocation, and consequently there is an opportunity for knowledge of intervention assignment to influence outcomes, particularly for self-reported outcomes. Because self-reported outcomes are distinct from performance measurement,[47,48] a repeat of this study focusing on objective measures of pain and physical function might yield new insight. However, the self-reported outcomes evaluated here are reliable, valid, and widely used in investigating OA.[49] Inclusion of a variety of control groups increased heterogeneity, which likely increased the variability and potentially reduced the magnitude of ES estimates. Despite this, moderate treatment effects were observed. By including a variety of comparator groups, we likely account for confounding factors, as well as studies demonstrating negative or weak effects (ie, reduced risk of publication bias). A detailed analysis evaluating the different comparator groups would yield greater insight; however, such an analysis is beyond the current study. Lastly, there were relatively few studies evaluating the hip. Therefore, findings from some of the analyses, such as the meta-regressions evaluating the associations with total volume and participant adherence, could not be completed due to a limited sample size.

In the management of knee and hip OA, clinicians can recommend that patients will benefit from resistance exercise programs lasting three to six months in duration but have flexibility in the total exercise volume to optimize improvements in pain and physical function. Although no recommendations can be made for longer duration exercise programs, further work can elucidate whether maintaining exercise for over a year confers broad health benefits compared to those that exercise for short durations.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr Maly had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Marriott, Hall, Bennell, Maly.

Acquisition of data. Marriott, Maciukiewicz, Almaw, Wiebenga, Ivanochko, Rinaldi, Tung.

Analysis and interpretation of data. Marriott, Hall.

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