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SUBGROUPING AND TARGETED EXERCISE PROGRAMMES FOR KNEE AND HIP OSTEOARTHRITIS (STEER OA) INDIVIDUAL PARTICIPANT DATA META-ANALYSIS. PROGRESS UPDATE AND SELECTION OF POTENTIAL MODERATORS FOR ANALYSES

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Purpose: Therapeutic exercise is recommended as a core treatment for adults with knee and hip osteoarthritis (OA). However, its average effect sizes for pain and physical function within randomised controlled trials (RCTs) tend to be small to moderate compared to no exercise controls. This may be due to insufficient targeting of exercise to specific subgroups (moderators), and/or that exercise programmes may not sufficiently address factors leading to improvement (mediators). This study aims to identify moderators and mediators of the effect of therapeutic exercise for reducing pain and improving physical function in people with knee or hip OA. This could lead to better targeting and refinement of future exercise interventions.

Methods: Systematic review update and individual participant data (IPD) meta-analyses, with ongoing patient and public involvement and engagement (PPIE) (PROSPERO: CRD42017054049). The search strategy from a previous systematic review (Uthman et al 2013) that identified 60 RCTs of exercise for people with knee or hip OA was rerun from March 2012 (previous search date) in 10 electronic databases. Identified titles, abstracts and subsequent full texts were reviewed against inclusion/exclusion criteria by two independent reviewers. In collaboration with the OA Trial Bank, leads of included RCTs are being invited to share their IPD. All meta-analyses, apart from mediation analyses, will use a two-stage approach, where estimates are obtained for each trial and then synthesised using a random effects model. Mediation analyses will use Causal Mediation Analyses. All meta-analyses will be on an intention-to-treat principle with summary estimates reported as standardised mean differences with 95% confidence intervals. To identify potential moderators for analyses, RCT leads (n=24) and PPIE representatives (n=4) who were named co-authors on the STEER OA protocol manuscript (collaborators) were invited to participate in a "moderator ranking exercise". Initially, collaborators were invited to a face-to-face meeting at Keele University where, through discussion, a list of 43 potential moderators of the effect of exercise was developed. Collaborators were then contacted via email or post, and asked to rank which moderators they believed were the 10 "most important". RCT leads were also asked to state their hypothesised direction of effect on pain and function outcomes for each selected moderator. Frequency counts were completed to identify the 10 moderators most commonly rated as "most important". Based on previous systematic review findings (Runhaar et al 2015), meta-analyses will explore the potential mediating effects of muscle strength (for knee and hip OA), proprioception (for knee OA) and extension deficits (for knee OA) in the association between therapeutic exercise and pain and physical function.

Results: The systematic review update identified 3943 unique references, which reduced to 272 following title and abstract screening. Remaining full texts were combined with those included in the original review (n=60) and nine identified from other sources, and were screened against the inclusion/exclusion criteria. In total, 114 RCTs met our criteria and are included in the review. In total, 60 RCT leads have agreed in principle to share IPD (approximately 8500 participants in total); 38 of these have signed data sharing agreements, and 28 datasets have been obtained to date. In total, 17 collaborators (13 RCT leads; 4 PPIE representatives) completed the "moderator ranking exercise". Overall, 11 subgroups were most frequently rated as being "most important" for moderating the effect of either pain or function following therapeutic exercise. These were: motivation to exercise; outcome expectations; pain severity; body mass index (BMI); anxiety/depression; self-efficacy; lower limb muscle strength; co-morbidity; age; instability (buckling); and baseline physical activity. These subgroups will therefore all be included in the analyses for both pain and function outcomes. The hypothesised direction of effect for some potential moderators was variable (see Table 1).

Conclusions: This is the first study, of this scale, to combine IPD from existing RCTs of therapeutic exercise for hip and knee OA. This will increase the statistical power to identify moderators and mediators of the effect of exercise. The moderators rated as "most important" will be explored in the IPD meta-analyses for both pain and function outcomes. The variation in hypothesised direction of effect of some potential moderators may reflect the lack of previous robust evidence in this area.

Table 1: RCT leads (n=13) hypothesised direction of effect on pain and function outcomes for each selected moderator

	PAIN OUTCOME		FUNCTION OUTCOME	
	Greater effect from exercise in those with greater*	Greater effect from exercise in those with lower*	Greater effect from exercise in those with greater*	Greater effect from exercise in those with lower*
Motivation to exercise	9 (100%)	0	9 (100%)	0
Outcome expectations	7 (100%)	0	8 (100%)	0
Pain severity	6 (86%)	1 (14%)	3 (50%)	3 (50%)
Body Mass index	3 (50%)	3 (50%)	5 (71%)	2 (29%)
Anxiety/depression	1 (11%)	8 (89%)	0	6 (100%)
Self-efficacy	7 (100%)	0	6 (100%)	0
Lower limb muscle strength	3 (43%)	4 (57%)	4 (44%)	5 (56%)
Co-morbidity	1 (17%)	5 (83%)	3 (60%)	2 (40%)
Age	3 (75%)	1 (25%)	3 (60%)	2 (40%)
Instability (buckling)	3 (100%)	0	2 (50%)	2 (50%)
Baseline physical activity	0	3 (100%)	1 (17%)	5 (83%)

* Numbers do not equal total (n=13) due to missing data

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EFFECT OF EXERCISE ON PSYCHOLOGICAL WELL-BEING IN PEOPLE WITH KNEE OSTEOARTHRITIS: SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

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Purpose: People with knee osteoarthritis (OA) often report poor psychological well-being. Although exercise is universally recommended by clinical guidelines to reduce knee OA symptoms, the effect of exercise on psychological health is less well understood in people with knee OA. The primary aim of this systematic review was to determine the effect of land-based exercise interventions on measures of psychological wellbeing (including depression, anxiety, self-efficacy and general mental health) in people with knee OA. The secondary aim was to investigate differential effects of exercise type on measures of psychological wellbeing.