ARTICLE IN PRESS

Osteoarthritis and Cartilage xxx (xxxx) xxx–xxx

Osteoarthritis and Cartilage

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Review

OARSI year in review 2023: Rehabilitation and outcomes

E.M. Macri [#] [†] [*], R.W. Selles [‡] [§], J.J. Stefanik [¶], M. Reijman [#]

Department of Orthopaedics and Sports Medicine, Erasmus MC, University Medical Center Rotterdam, the Netherlands
† Department of General Practice, Erasmus MC, University Medical Center Rotterdam, the Netherlands
‡ Department of Plastic, Reconstructive and Hand Surgery, Erasmus MC, Rotterdam, the Netherlands
§ Department of Rehabilitation Medicine, Erasmus MC, Rotterdam, the Netherlands
¶ Department of Physical Therapy, Movement and Rehabilitation Sciences, Northeastern University, Boston, MA, USA

ARTICLE INFO

Article history:
Received 27 June 2023
Accepted 31 August 2023

Keywords:
Rehabilitation
Exercise
Education
Weight loss
Adjuncts
Review

SUMMARY

Objective: We systematically reviewed the literature to identify comparative studies of core treatments (exercise, education, or weight management), adjunct treatments (e.g. electrotherapeutical modalities, bracing), or multimodal treatments (core plus other treatments), for treating osteoarthritis (OA) complaints, published between 1 March 2022 and 1 March 2023.

Design: We searched three electronic databases for peer-reviewed comparative studies evaluating core treatments, adjunct treatments, or multimodal treatments for OA affecting any joint, in comparison to other OA treatments. Two authors independently screened records. Methodological quality was assessed using the Physiotherapy Evidence Database (PEDro) scale. A narrative synthesis focusing on pain and function outcomes was performed in studies with a mean sample size of at least 46 participants per treatment arm.

Results: 33 publications (28 studies), 82% with PEDro ratings of good or excellent, were eligible for narrative synthesis: 23 studies evaluated knee OA; one knee OA or chronic low back pain; two knee or hip OA; one hip OA only; and one thumb OA. No studies identified a dose, duration or type of exercise that resulted in better pain or function outcomes. Core treatments generally showed modest benefits compared to no or minimal intervention controls.

Conclusions: Rehabilitation research continues to be focused on the knee. Most studies are not adequately powered to assess pain efficacy. Further work is needed to better account for contextual effects, identify treatment responder characteristics, understand treatment mechanisms, and implement guideline care.

Introduction

Many clinical practice guidelines are available to manage osteoarthritis (OA) affecting the hips and knees, and fewer so for hand OA.[1–9] Unfortunately, there are some inconsistencies across these guidelines, which can confuse clinicians and researchers. To help clarify and provide more insight into optimal evidence-based OA management approaches, several publications this year critically evaluated and compared the different clinical practice guidelines.[10–18] These evaluations concluded that guidelines generally agree on a core treatment approach of exercise and education, with the addition of weight management in individuals with hip or knee OA who are overweight or obese. This conclusion is supported by a large amount of literature in favor of exercise for managing both knee and hip OA.[19,20] However, guideline recommendations diverge beyond core treatments. For example, there is little agreement among clinical practice guidelines regarding adjunct therapies commonly used in rehabilitation settings, such as electrotherapeutic modalities, manual therapy, or the use of devices like bracing or orthoses. Moreover, guidelines generally lack details about how best to deliver core or adjunct treatments. This is likely on account of a lack of evidence investigating: the optimal dose or type of exercises; primary efficacy for the design and delivery of education and weight management; or what mode of delivery (e.g., group vs. individualized, face-to-face vs. online) is best. Long-term outcomes of both core and adjunct treatments have also rarely been evaluated. More research is needed to address these gaps and to clarify optimal evidence-based approaches to managing OA.

For the present Year in Review, we systematically reviewed the literature to identify publications of comparative studies of core

* Correspondence to: Dr. Molewaterplein 40, 3015 GD Rotterdam, the Netherlands.
E-mail addresses: e.macri@erasmusmc.nl (E.M. Macri), r.selles@erasmusmc.nl (R.W. Selles), j.stefanik@northeastern.edu (J.J. Stefanik), m.reijman@erasmusmc.nl (M. Reijman).

https://doi.org/10.1016/j.joca.2023.08.011

Please cite this article as: E.M. Macri et al., OARSI year in review 2023: Rehabilitation and outcomes, Osteoarthritis and Cartilage, https://doi.org/10.1016/j.joca.2023.08.011

treatments (exercise, education, or weight management), adjunct treatments (e.g. electrotherapeutical modalities, bracing), or multimodal treatments (combining core with adjunct treatments) for OA complaints, published between 1 March 2022 and 1 March 2023. We then performed an analysis and narrative synthesis of a subset of the eligible studies of sufficiently large sample size.

Methods

Study selection

We searched MEDLINE (OVID), EMBASE (OVID), and CINAHL (EBSCOhost) databases for peer-reviewed studies evaluating core or adjunct treatments for OA affecting any joint, in comparison to other OA treatments (e.g., exercise, surgery, or pharmaceutical), placebo/sham, usual care, or waitlist/no treatment (see eligibility criteria, Table 1). We included comparison studies only, meaning we included clinical trials (randomized, non-randomized) as well as observational studies in which at least two types of treatment were compared. We limited our search to English language publications. We developed our search terms in consultation with a health sciences librarian (W Bramer) with considerable skill and experience (see supplementary materials for search terms).

Electronic records captured from the search of all three databases were uploaded and combined into a single reference library using Endnote 20 and were subsequently deduplicated. We then uploaded all records into Covidence (Veritas Health Innovation, VIC, Australia). Each title/abstract was then screened by two independent screeners (any two of the four coauthors), followed by full text screening by two independent screeners. In the case of disagreements, a third screener (EMM) led conflict resolution in consultation with all coauthors.

Study quality

We evaluated study quality using two quality indicators. The first indicator was sample size. Adequate power will differ among studies based on specific research aims, expected outcomes, and other factors. However, we decided upon a minimum sample size threshold that would enable us to identify studies more likely to be powered to evaluate pain, our main outcome of interest. This threshold was extracted from one of this year's published studies that calculated power based on targeted pain outcomes.[21] Specifically, a threshold of at least 46 participants per treatment arm was determined based on a target between-group difference of at least a minimal important change (MIC) of 1.8/10 on a numeric pain rating score.[21] A secondary threshold of at least 90 participants per treatment arm was also extracted from a publication in which the target between-group difference was at least an SMD of 0.4, consistent with what would be expected of a knee OA exercise trial.[22]

The second quality indicator was obtained from the Physiotherapy Evidence Database (PEDro),[23] from which we extracted PEDro quality scores. The PEDro scale is an 11-item tool, and studies with scores from 0 to 3 are considered to be 'poor', 4–5 'fair', 6–8 'good', and 9 or higher are considered 'excellent'.[24] In cases where no PEDro score was available on the website for a given record, we rated the PEDro scores ourselves. Specifically, two raters (RWS, and MR) independently scored PEDro ratings, and a third rater (EMM) was consulted to resolve disagreements.

Data extraction and analysis

For the present manuscript, we only extracted and synthesized results from studies that met the minimum average sample size per treatment arm of at least 46. From these studies, we extracted participant demographics (age, sex, body mass index (BMI), OA joint affected), study type, interventions evaluated including dose, and sample size. We reported sample size based on the number of participants included in the analysis from which we extracted results, so in completed case analyses this was the sample size with complete data, while in intention-to-treat studies this was the baseline sample size. Participant demographics were reported at the study level, i.e., combining treatment arms. All data extraction was performed by one coauthor and verified by a second coauthor.

Although we did not limit our search according to outcomes, we reported mainly self-reported pain and self-reported function in primary efficacy studies or subsequent follow-up studies. We also highlighted additional outcomes in cases such as secondary responder or mediation analyses, cost-effectiveness studies, or other outcomes of unique clinical interest. In studies where more than one measure of pain or function was evaluated, we extracted only one variable for each domain, based on current recommended hierarchies for pain and function variables.[25,26] We extracted the pain and function outcomes immediately post-treatment in primary efficacy studies (i.e., no results following the discontinuation of treatment), and prioritized extracting absolute scores when available, only extracting change scores when absolute scores were not reported. We calculated and reported between-group effect sizes as Hedge's standardized mean difference (SMD) with 95% confidence intervals (95% CI) to facilitate comparisons across studies. We interpreted SMDs ≤0.3 as small, 0.4–0.7 as moderate, and ≥0.8 as large effect sizes.[27] We undertook a narrative synthesis of the included

Concept	Eligibility criteria
Population	Osteoarthritis defined as joint pain in adults >45 years old (regardless of whether imaging was required for diagnosis and who diagnosed participants)
Intervention	Exercise, education, weight management, and adjunct physical or behavioral therapies (e.g., bracing, electrotherapeutic modalities, manual therapy, cognitive behavioural therapy, etc). We excluded surgical, pharmacological, and alternative/complimentary treatments.
Comparison	Any comparision treatment. This could include any rehabilitation treatment, but also surgical, pharmacological, placebo/sham, wait and see, or usual care.
Outcomes	Any OA-related outcomes. This could include clinical outcomes (pain, function), structural (e.g. imaging findings), process outcomes (e.g. adherence, acceptability), or cost-effectiveness. We excluded outcomes relating to other comorbidities (e.g. fracture risk)
Study designs	Comparative designs, including randomized clinical trials (RCTs) or observational studies with multiple treatment arms. We excluded case studies, case series, non-interventional studies, reviews, clinical practice guidelines, and protocols.
Languages	English
Publication dates	1 March 2022 to 1 March 2023

Table 1

Osteoarthritis and Cartilage

studies, because a meta-analysis of only a single years' worth of publications is not clinically useful. All statistical analyses were performed using Stata SE 17.0 (StataCorp LLC, College Station, TX, USA).

Results

The initial search yielded 4865 records (see Fig. 1).[28] Following screening we identified 133 publications of 128 unique studies that met our search eligibility criteria. Most of these publications (117) focused on the lower extremity (103 knee, four knee or hip, seven hip, one knee or low back, one first metatarsophalangeal (great toe), and one patellofemoral joint); eleven focused on the upper extremity (four hand, seven thumb); and five focused on the spine (three cervical, two lumbar). Of the 133 eligible publications, 33 analyzed sample sizes of ≥46 per treatment arm and were thus included in further analysis in the present study (see Supplementary S2 for references of studies not included in the analysis). These 33 publications analyzed 28 unique datasets/studies, of which 23 studies evaluated knee OA alone; one evaluated knee OA or chronic low back pain; two evaluated knee or hip OA; one evaluated hip OA only; and one evaluated first carpometacarpal joint (thumb) OA. Nineteen of the 33 publications (16 studies) had mean samples of ≥90

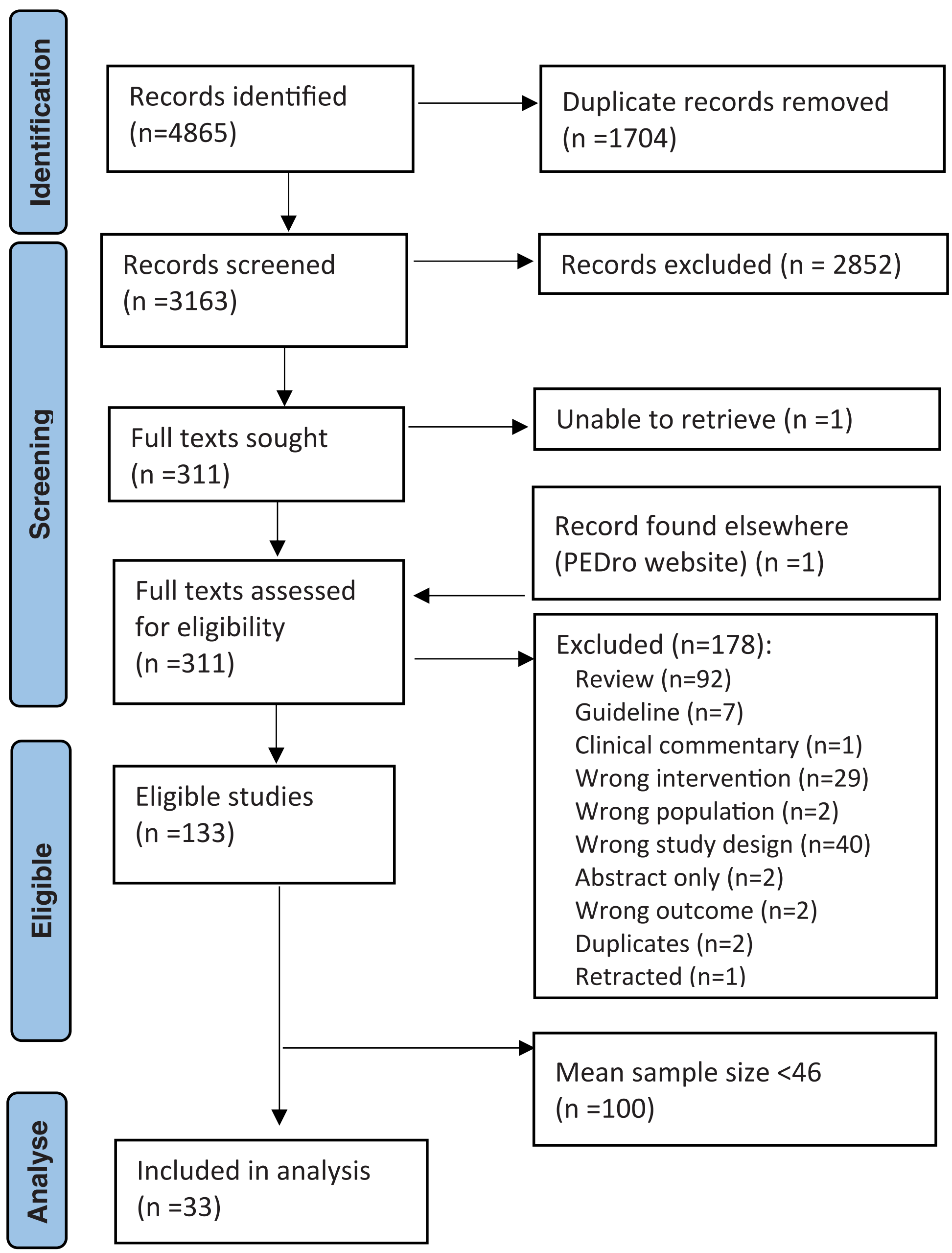

Fig. 1 Osteoarthritis and Cartilage

Flow chart of search for eligible publications.

First author	PEDro score	Random	Sample size*	Population (diagnosis)	Age mean (SD) years	Women n (%)	BMI mean (SD) kg/m^2	Interventions	Pain Between-group SMD (95%CI)	**Function** Between-group SMD (95%CI)**
Core treatments in comparison to no or minimal interventions										
Bennell[29,30]	7	Yes	414	Knee OA (NICE), overweight/obese	64.8 (8.2)	227 (55%)	33.2 (3.5)	6-month program: (1) diet & exercise (2) exercise (3) website control	NRS (1) vs. (2) **-0.32 (−0.53, −0.10)** (1) vs. (3) **-0.76 (−1.05, −0.47)** (2) vs. (3) **-0.46 (−0.74, −0.17)**	WOMAC Function (1) vs. (2) **-0.24 (−0.45, −0.03)** (1) vs. (3) **-0.99 (−1.28, −0.69)** (2) vs. (3) **-0.72 (−1.01, −0.43)**
Bennell[22]	7	Yes	212	Knee OA (NICE)	62.3 (7.7)	148 (70%)	30.3 (5.5)	12-week program: (1) online yoga program plus website education (2) website only	WOMAC Pain -0.17 (−0.44, 0.10)	WOMAC Function **-0.31 (−0.59, −0.04)**
Henriksen[42,43]	(7)^	Yes, follow-up	206	Knee OA (ACR and KL≥2)	68.4 (8.5)	94 (46%)	27.3 (3.6)	8-week program: (1) GLAD exercise and education (2) open label saline injections	See primary findings[56] 1 year follow-up: ΔKOOS Pain -0.08 (−0.35, −0.20)	See primary findings[56] 1 year follow-up: ΔKOOS ADL 0.06 (−0.22, 0.33)
Hunter[31]	9	Yes	217	Knee OA (NICE)	64.5 (range 45 – 95)	131 (60%)	≥27 kg/m^2: 122 (56%)	12-month program: (1) education with OA action plan for exercise and weight management (2) usual primary care	KOOS Pain -0.12 (−0.40, 0.14)	KOOS ADL **-0.27 (−0.54, −0.001)**
Messier[37]	7	Yes	645	Knee OA (ACR), overweight/obese	64.6 (7.8)	637 (77%)	36.8 (6.9)	18-month program: (1) diet & exercise (2) attention control	WOMAC Pain **-0.13 (−0.27, 0.00)**	WOMAC Function **-0.23 (−0.36, −0.09)**
Kaufman[33]	5	Yes, 2' analysis	345	Knee OA (medical records), veterans	60.0 (10.3)	45 (13%)	NR	9-month program: (1) exercises delivered online, progress non-responders to phone coaching; progress non-responders again to in-person physiotherapy (2) education	See primary findings[59]	See primary findings[59]
Robson[53]	(7,8)	Yes, 2' analysis	160 (LBP) 120 (knee OA)	Knee OA or chronic LBP, overweight or obese	Knee 61.6 (12.6) LBP 56.7 (13.4)	Knee 74 (62%) LBP 94 (59%)	Knee 32.7 (3.3) LBP 32.3 (3.5)	6-month program: (1) telephone-based lifestyle weight loss coaching service (2) usual care, surgical wait-list	See primary findings[57,58]	See primary findings[57,58]
Core treatments in comparison with other core treatments										
de Zwart[49,50]	9	Yes	177	Knee OA (ACR)	67.6 (5.8)	107 (60%)	28.2 (4.4)	Exercise 12 weeks: (1) high intensity (70–80% of 1-rep max) (2) low intensity (40–50% of 1 rep max)	NRS 0.09 (−0.21, 0.39)	WOMAC Function 0.03 (−0.26,0.33)
Aree-Ue[47]	5	Yes	110	Knee OA (ACR), overweight and Type 2 diabetes	60–74: 92(84%) ≥75: 18 (16%)	95 (86%)	W: 60.5 (11.6) kg	Education (3 days) and exercise (6 months): (1) with peer-support (2) without peer-support	NRS **-0.52 (−0.90, −0.14)**	.
Cagnin[48]	4	Yes, 2' analysis	163	Knee OA (KL≥2)	62.8 (8.7)	105 (64%)	29.7 (5.1)	6-month program: (1) primary care, personalized recommendations and exercise, education (2) primary care, personalized recommendations and exercise (3) primary care	See primary findings[55]	See primary findings[55]

(continued on next page)

Table 2 (*continued*)

First author	PEDro score	Random	Sample size*	Population (diagnosis)	Age mean (SD) years	Women n (%)	BMI mean (SD) kg/m^2	Interventions	Pain Between-group SMD (95%CI)	**Function** Between-group SMD (95%CI)**
Heikkinen[52]	(6,8)	Yes (2 RCTs), 2' analysis	160	Mild Knee OA (KLI,II), postmenopausal women	61.2 (4.4)	160 (100%)	26.1 (3.6)	Exercise program: (1) 4-month aquatic rehabilitation (2) 12-month land based exercises (3) usual care	ΔKOOS Pain (1) vs. (2) 0.08 (−0.37, 0.53) (1) vs. (3) -0.29 (−0.66, 0.08) (2) vs. (3) -0.39 (−0.79, 0.01)	.
Husted[51]	7	Yes	140	Knee OA awaiting arthroplasty (KL≥2)	66.7 (9.9)	76 (54%)	W: 91.9 (19.9) kg H: 1.69 (0.83) m	Seated knee extension, 12 weeks: (1) six times/week (2) four times/week (3) two times/week	ΔKOOS Pain (1) vs. (2) 0.16 (−0.25, 0.57) (1) vs. (3) 0.34 (−0.07, 0.75) (2) vs. (3) 0.20 (−0.20, 0.61)	ΔKOOS ADL (1) vs. (2) 0.13 (−0.27, 0.54) (1) vs. (3) 0.24 (−0.17, 0.65) (2) vs. (3) 0.11 (−0.30, 0.51)
Jönsson[32]	5	No, 2' analysis	6946	Knee OA (64%), Hip OA (36%) (Swedish National Board of Health and Welfare)	67 (9)	4952 (71%)	27.5 (4.8)	Exercise and education 12 weeks: (1) smart phone app (2) face to face	NRS **-0.46 (−0.50, −0.41)**	.
Knoop[34,35]	9	Yes	328	Knee OA (ACR)	64.9 (9.0)	209 (64%)	27.9 (4.6)	12-week program: (1) stratified care (high strength, low strength, and obese subgroups) (2) usual physiotherapy	NRS 0.00 (−0.22, 0.22)	KOOS ADL 0.05 (−0.16, 0.27)
Roesel[41]	5	No, 2' analysis	657	Knee OA or Hip OA (diagnosed by medical practitioner)	62.6 (10.3)	469 (71.4%)	27.9 (4.7)	3-month program: (1) home-based mixed training (strength, flexibility, motor learning, posture) (2) machine-based strength training only	WOMAC Pain -0.08 (−0.27, 0.11)	WOMAC Function 0.07 (−0.12, 0.26)
Torstensen[45]	9	Yes	189	Knee OA (KL≥1)	62.1 (9.3)	106 (56%)	28.0 (4.1)	Exercise 12 weeks: (1) high dose (11 exercises) (2) low dose (5 exercises)	KOOS Pain -0.05 (−0.34, 0.23)	KOOS ADL -0.21 (−0.49, 0.08)

PEDro = Physiotherapy Evidence Database score; BMI = body mass index; SMD = Standardized Mean Difference, Hedge's g; ACR = American College of Rheumatology; KL = Kellgren & Lawrence; OA = osteoarthritis; LBP = low back pain; W = weight; H = height; f/u = follow-up; s = seconds; y = years; KOOS=Knee injury and Osteoarthritis Outcomes Score; ADL = function in activities of daily living; NRS = Numeric Pain Rating Scale; WOMAC = Western Ontario McMaster Osteoarthritis Questionnaire; Δ= change; NR = not reported; RCTs, randomized clinical trial.

Bold = p < 0.05

^(n) = PEDro scores available for original/related primary publication

*sample size analyzed immediately post-treatment (e.g., for intention-to-treat studies, it is the same as the number randomized)

**SMD, negative values indicate more favorable outcome (less pain, higher function) than comparison group

Table 2

Osteoarthritis and Cartilage

Core treatments: any combination of exercise, education or weight management.

per treatment arm[22,29–46]. PEDro scores were rated as fair in six publications, good in 16 publications, and excellent in 11 publications (see Table 2).

Core treatments

Twenty publications of 16 unique studies evaluated one or more core treatments,[22,29–35,37,41–43,45,47–53] three of which used data from studies where primary findings had been published prior to this past year.[33,54,55] All studies evaluated treatments in individuals with knee OA, though two studies also included hip OA[32,41] and one included chronic low back pain.[53]

Core treatments in comparison with no or minimal intervention controls

This year's primary efficacy studies of core treatments evaluated treatments ranging in duration from 12 weeks to 18 months. Four studies evaluated core treatments ranging from 12 weeks to 18 months in comparison to no or minimal interventions (see Table 2).[22,29,31,37] Four additional publications provided additional analyses on previously published studies that had compared core treatments to no or minimal intervention care.[33,42,43,53]

One study evaluated a 12-month telehealth-delivered guideline care program (education, exercises, and weight management) offered through general practitioner referral to centralized care support teams, compared to usual primary care.[31] Although the guideline care group had better function following treatment, the effect size was small and of doubtful clinical importance. A six-month unsupervised online yoga program did not result in between-group differences in pain, though function was better (small to moderate effect size), compared to web-based educational materials.[22] A six-month program of physiotherapy-led, telehealth-delivered exercises, on the other hand, showed moderately better pain and function compared to web-based educational materials in individuals who were overweight or obese.[29] A third arm of this same trial added diet to the exercise program, resulting in small SMDs of better pain and function compared to the exercise-alone group, and moderate to large SMDs for pain and function compared to educational controls. Moreover, the diet and exercise group lost 8.1 (95%CI 6.8, 9.4) kg more than exercise alone, and 9.3 (7.5, 11.2) kg more than controls. The authors concluded that the supervised online program was cost-effective, accessible, and potentially scalable.[30] Another diet and exercise program, this one 18 months long, resulted in negligible to small reductions in pain and function, and 6 (95%CI 4.7, 7.3) kg more weight loss compared to an attention control group.[37] Moreover, on account of a 24% reduction in pain in the control group, authors in this study acknowledged that a large portion of the effects within each group were likely due to contextual effects (i.e., regression to the mean) more so than true treatment effects.

One follow-up study published this year extended the findings of a previous publication in which exercise and education had not differed from open-label placebo in pain or function.[42,55] This one-year follow-up continued to show no between-group differences[42]. Further analysis of this dataset revealed that individuals may be more likely to respond to treatment if at baseline they were taking analgesics or reported constant pain.[43] A secondary analysis of two other previously published studies of weight management coaching in overweight or obese individuals with knee OA[56] or chronic low back pain[57] found no difference in pain and function between compliers and non-compliers.[53] Finally, cost-effectiveness was established for a previously published study in which veterans received progressively higher levels of supervision in performing exercises, as needed, in comparison to educational controls, an approach that was previously found to be beneficial for pain and function.[33,58]

Core treatments in comparison with other core treatments

Four new studies (six publications) evaluated different doses, volumes, or types of exercise programs[34,35,45,49–51]; four publications provided additional analyses on studies published prior to the past year[32,41,48,52]; and two studies compared different modes of delivery of the same core treatment programs.[32,47] Programs ranged from three to six months long and all studies investigated knee OA except one study that also included hip OA.[41] The only studies reporting significant findings were in the two studies comparing different treatment delivery modalities. Specifically, one study found that adding trained peer-support staff to a six-month exercise program for knee OA resulted in moderately less pain than the same program without peer-support (SMD −0.5 [95%CI −0.9, −0.1).[47] The second study compared two separate large knee or hip OA cohorts, both of which received exercise and education[32]: one cohort (Joint Academy)[59] received treatment through a smart phone app, while the other cohort (Better Management of Patients with OA)[60] received face-to-face care. Authors found moderately lower pain in favour of the smart phone delivery mode (SMD −0.4 [95%CI −0.5, −0.4]). No significantly different SMDs in pain or function were found among the remaining studies, including: high intensity compared to low intensity exercise[49]; a high dose compared to low dose exercise program[45]; aquatic rehabilitation compared to land-based exercises[52]; a single leg extension exercise performed between 2 and 6 times per week[51]; stratifying care according to strength and obesity in comparison to usual physiotherapy[34,35]; or home-based mixed exercises (strength, flexibility, etc) compared to machine-based strength training.[41]

Despite negative pain and function findings among so many studies, two publications this year found differences in secondary outcomes that may imply treatment effects on joint health,[48,50] and one study identified baseline characteristics associated with better treatment response.[41,43] First, in the high vs. low intensity exercise study, blood samples were collected in order to measure human ARGS (huARGS), C2M, and PROC2 serum biomarkers, which relate to cartilage tissue turnover.[50] Both huARGS and C2M increased within groups following treatment, suggesting an increase in cartilage turnover or degradation, though only huARGs showed between-group differences at follow-up, with higher huARGs levels in the high intensity group. Given the lack of clinical benefit of high intensity exercise, and until it is better understood what these biomarker findings mean in terms of OA processes, the authors cautioned against high intensity exercise programs in individuals with knee OA. In a second study, biomechanical features were evaluated from a previously published study in which primary care plus personalized exercise and education had shown better pain and function than primary care alone.[48,54] This publication showed that the group receiving exercise and education had 2.5 (95%CI 1.3, 4.7) times the odds of improving biomechanical features when compared to primary care alone.[48,54] Finally, a secondary analysis of two primary exercise studies, one evaluating home-based exercises[61] and one machine-based strength training,[62] found that individuals with more severe symptoms experienced the largest improvements in pain and function following either exercise program.[41]

Adjunct treatments

Eight publications of seven unique studies evaluated adjunct therapies (Table 3). All studies evaluated various electrotherapy modalities, except one that compared two acupuncture approaches.[36] All studies investigated individuals with knee OA except one that investigated hip OA.[63]

Six electrotherapy modality publications (five studies) compared active treatments to sham,[38,63–67] and one compared two different modalities.[68] Two sham-controlled studies reported negative results,

Table 3

Adjunct treatments: electrotherapy modalities or acupuncture.

First author	PEDro score	Random	Sample size	Population (diagnosis)	Age mean (SD) years	Women n (%)	BMI mean (SD) kg/m^2	Interventions	Pain SMD (95%CI)	Function SMD (95%CI)
Jia[68]	8	Yes	114	Knee OA (KL1–3)	61.1 (10.0)	87 (76%)	25.2 (3.0)	12 day program: (1) focused pulsed low-intensity ultrasound (2) pulsed shortwave diathermy	WOMAC Pain **-0.89 (−1.28, −0.51)**	WOMAC Function **-1.09 (−1.48, −0.69)**
Liu[36]	8	Yes	666	Knee OA (KL0–3, Chinese Diagnostic Guidelines)	60.7 (8.8)	535 (80%)	24.1 (3.0)	4 week program: (1) acupuncture on lower pain threshold points, 12 sessions (2) acupuncture on higher pain threshold points, 12 sessions (3) wait list	WOMAC Pain (1) vs. (2) -0.00 (−0.19, 0.19) (1) vs. (3) **-0.29 (−0.48, −0.10)** (2) vs. (3) **-0.29 (−0.48, −0.10)**	WOMAC Function (1) vs. (2) 0.05 (−0.13, 0.24) (1) vs. (3) -0.27 (−0.45, −0.08) (2) vs. (3) **-0.31 (−0.50, −0.13)**
Martorella[64,65]	11	Yes	120	Knee OA (ACR)	66.0 (8.4)	82 (68%)	32.6 (8.5)	3 week program: (1) self-administered transcranial direct current stimulation (2) sham stimulation	ΔNRS **-1.19 (−1.58, −0.80)**	.
Reichenbach[38]	9	Yes	220	Knee OA (KL≥2)	65.6 (10.1)	112 (51%)	27.2 (4.9)	3 week program: (1) TENS (2) sham TENS	WOMAC Pain -0.09 (−0.35, 0.18)	WOMAC Function -0.04 (−0.31, 0.22)
Sawitzke[66]	10	Yes	132	Knee OA (KL1–3), Veterans	63.6 (10.7)	13 (10%)	31.7 (5.5)	48 week program, self-administered: (1) pulsed low-intensity ultrasound (2) sham ultrasound	WOMAC Pain -0.03 (−0.38, 0.31)	WOMAC Function -0.01 (−0.35, 0.33)
Sax[67]	7	Yes	156	Knee OA (KL2–4)	61.1 (10.4)	72 (46%)	31.6 (6.0)	12 week program, self-administered: (1) neuromuscular stimulation (2) sham stimulation	ΔWOMAC Pain -0.21 (−0.55, 0.13)	ΔWOMAC Function **-0.45 (−0.79, −0.11)**
Şah[63]	10	Yes	148	Hip OA (KL2–3)	63.8 (6.2)	98 (66%)	26.7 (2.1)	4 week program: (1) focused Extracorporeal Shock Wave Therapy (ESWT) (2) radial ESWT (3) sham ESWT	WOMAC Pain (1) vs (2) **-0.60 (−0.98, −0.21)** (1) vs (3) **-0.91 (−1.31, −0.51)** (2) vs. (3) **-0.42 (−0.80, −0.03)**	WOMAC Function (1) vs (2) **-0.53 (−0.91, −0.15)** (1) vs (3) **-0.73 (−1.12, −0.33)** (2) vs. (3) -0.26 (−0.64, 0.13)

PEDro = Physiotherapy Evidence Database score; BMI = body mass index; SMD = Standardized Mean Difference; ACR = American College of Rheumatology; KL = Kellgren & Lawrence; OA = osteoarthritis; W = weight; H = height; f/u = follow-up; s = seconds; y = years; KOOS=Knee injury and Osteoarthritis Outcomes Score; ADL = function in activities of daily living; NRS = Numeric Pain Rating Scale; WOMAC = Western Ontario McMaster Osteoarthritis Questionnaire; Δ= change; TENS = transcutaneous electrical stimulation; ESWT = extracorporeal shock wave therapy.
^(n) = PEDro scores available for original/related primary publication
*sample size analyzed immediately post-treatment (e.g., for intention-to-treat studies, it is the same as the number randomized)
**SMD, negative values indicate more favorable outcome (less pain, higher function) than comparison group
Bold = p < 0.05

Osteoarthritis and Cartilage

one showing no difference in pain or function with three weeks of transcutaneous electrical stimulation (TENS)[38]; the other showing no differences with 48 weeks of pulsed low-intensity ultrasound.[66] The latter study also found no between-group differences in cartilage biomarkers (Coll2–1, Coll2–1 NO2, COMP, CTX-II, C) or cartilage thickness.[66] However, a second study investigated just 12 days of pulsed low-intensity ultrasound and found lower pain and higher function compared to a group receiving pulsed shortwave diathermy.[68] Other sham-controlled studies found between-group differences, including small to moderately better pain and function using neuromuscular stimulation for 12 weeks[67]; moderate to large differences in pain and function in hip OA favoring four weeks of focused extracorporeal shockwave therapy (ESWT) more so than radial ESWT which was in turn moderately better for pain than sham[63]; and a large difference in pain following three weeks of transcranial direct current stimulation.[64,65] The latter study also found improved pain sensitization in the active treatment arm on quantitative sensory testing including heat pain threshold, heat pain tolerance, pressure pain threshold, and conditioned pain modulation.[65]

The single acupuncture study found no difference administering acupuncture to higher compared to lower pain threshold points, but both treatment groups had better pain and function compared to wait list controls.[36]

Multimodal treatments

Five studies evaluated multimodal treatments, meaning one or more core treatments in combination with another treatment modality (Table 4). Two studies reported pain and function immediately after treatment,[44,46] two reported five-year follow-ups of previously published studies,[40,69] and one performed secondary analyses on previously published data.[39] All studies investigated knee OA except one that investigated first carpometacarpal (thumb) OA.[46]

In a one-year retrospective comparison observational study, all male construction workers attended a three-week program of exercises, education, manual therapy, and electrotherapy modalities, followed by self-management and a one-week refresher.[44] During the one year of self-management, participants either performed exercises in a gym, at home, or they did not perform any exercises. Those who completed exercises in a gym environment throughout the year had lower pain and higher function than individuals who did not exercise. A secondary analysis of a previous study that had found no difference between physical therapy and internet-based unsupervised exercises, found that baseline characteristics of higher BMI, older age, longer disease duration, and being employed correlated with greater benefit from the additional supervision or treatment offered by physical therapy.[39,70]

A five-year follow-up study of individuals with degenerative meniscal tears found no long-term differences in pain or function between a group receiving early arthroscopic partial meniscectomy vs. a group receiving eight weeks of physiotherapy-delivered exercises with an option for delayed surgery.[40,71] This extended the original study's non-inferiority findings.[71] Another five-year follow-up study was published this year of the MEDIC study, which had originally found better pain and function in individuals who received 12 weeks of multimodal treatment compared to an educational leaflet control group.[69,72] At the five-year follow-up, there was no longer a difference between groups.[69] Importantly, the authors noted that both groups demonstrated substantial improvements in symptoms over the five-year period, possibly representing regression to the mean and calling into question the belief that OA progressively worsens over time.

The one study investigating individuals awaiting surgical consult for first carpometacarpal OA compared 12 weeks of occupational therapy (OT)-delivered education along with a self-management program of exercises, orthoses, and assistive devices to a group provided a single OT education session.[46] On completion of the program, those offered the self-management program had lower pain and higher function than the single education session.

Discussion

The past year saw 133 new publications in the field of OA rehabilitation, approximately a quarter of which (n = 33) were of a sufficient sample size to be included in further analyses in the present review. No studies identified a specific dose, duration or type of exercise that resulted in better pain or function outcomes. A higher level of support or supervision appeared to be beneficial for certain patients, particularly those with baseline characteristics such as older age, higher BMI, longer duration symptoms, or being employed.[39,47,70] Individuals with more severe baseline symptoms were also more likely to respond to core treatments.[41] In terms of different modes of delivery, both online and app-delivered treatments were efficacious, more so when supervision or peer-support was integrated into the treatment delivery.[22,29,32,47] Core treatments generally showed modest benefits compared to no or minimal intervention controls, even when separately analyzing compliers and non-compliers.[22,29,31,37,42,53]

Among the seven adjunct therapy studies, one notable is the large sham-controlled randomized clinical trial (RCT) of transcutaneous electrical nerve stimulation (TENS), reportedly the first adequately powered TENS study, that found no difference in pain or function compared to sham.[38] This study may help to clarify conflicting conclusions regarding TENS efficacy currently found in the literature.[73,74] Also noteworthy were two publications of one study of transcranial direct current stimulation, which found large reductions in pain compared to sham and thus provides evidence for an as of yet not well-studied modality.[75,76] The remaining studies of adjunct therapies this year do not challenge or further clarify previous findings.[77–81]

Notable among multimodal interventions this year is the availability of longer-term evidence, one continuing to support that chronic meniscal tears do not require early surgical intervention,[40] and a second demonstrating that even individuals offered only education continue to improve substantially over time, calling into question the notion that OA symptoms universally worsen over time.[69]

Future directions in OA rehabilitation research

Englund and Turkiewicz published an important editorial this year,[82] inviting us into a deeper and perhaps uncomfortable conversation about the true efficacy of exercise in managing knee OA. Although the literature overwhelmingly concludes that exercise confers small to moderate effects on knee and hip OA symptoms and that no further trials are needed in comparison to no or minimal intervention trials,[19,20] the authors argue that the scientific community has not adequately considered contextual effects, including placebo and regression to the mean, when designing or interpreting results of exercise trials. Among others, they cite papers like Messier et al.[37] in which most improvements in both diet and exercise as well as attention groups were mostly contextual, and between-group differences were actually minimal; Messier et al. in which no difference was found between high-intensity exercise, low-intensity exercise, or even attention control groups[83]; and Bandak et al.[55] in which no difference was found between exercise and an open label saline injection. Common to these trials is that between-group

Table 4

Multimodal treatments: any combination of core treatment plus other treatment.

First author	PEDro score	Random	Sample size	Population (diagnosis)	Age mean (SD) years	Women n (%)	BMI mean (SD) kg/m²	Interventions	Pain SMD (95%CI)	Function SMD (95%CI)
Coffman[39]	(8)	Yes, 2' analysis	345	Knee OA (radiographic or physician-diagnosed)	65.3 (11.0)	247 (72%)	31.3 (8.0)	4-month program: (1) internet based exercises (2) physical therapy (exercise, manual therapy, assistive devices, electrotherapy modalities) (3) waitlist control	See primary findings[71]	See primary findings[71]
Larsen[690]	(8)	Yes, follow-up	100	Knee OA not eligible for arthroplasty (KL≥1)	66.0 (8.9)	51 (51%)	30.0 (5.4)	12-week program: (1) physical therapy & dietician (education, exercise, insoles, diet, pain medication) (2) educational leaflets	See primary findings[73] 5-year follow-up: ΔKOOS Pain 0.07 (−0.33, 0.46)	See primary findings[73] 5-year follow-up: ΔKOOS ADL -0.13 (−0.53, 0.26)
Noorduyn[40]	6	Yes, follow-up	319	Degenerative meniscal tears (confirmed on MRI)	58.0 (6.6)	161 (50%)	27.0 (3.9)	(1) arthroscopic partial meniscectomy (APM) (2) 8-week exercise-based physical therapy with optional delayed APM	See primary findings[72] 5-year follow-up: VAS -0.04 (−0.26, 0.18)	See primary findings[72] 5-year follow-up: KOOS-PS -0.16 (−0.38, 0.06)
Pietsch[44]	4	No	401	Knee OA (diagnostic codes)	50.0 (7.1)	0 (0%)	28.8 (4.3)	3-week knee-college (PT, electrotherapy and manual therapy, psychological health), with annual 1 week refresher plus 1 year of: (1) gym exercises (2) home exercises (3) no exercises	WOMAC Pain (1) vs. (2) -0.17 (−0.41, 0.06) (1) vs. (3) **-0.40 (−0.65, −0.16)** (2) vs. (3) -0.22 (−0.50, 0.05)	WOMAC Function (1) vs. (2) -0.12 (−0.36, 0.11) (1) vs. (3) **-0.32 (−0.56, −0.07)** (2) vs. (3) -0.19 (−0.46, 0.09)
Tveter[46]	7	Yes	180	1st carpometacarpal OA (referred for surgical consult)	63.1 (7.6)	142 (79%)	NR	12-week program: (1) OT education, exercises, orthoses, assistive devices (self-management) (2) wait list with 1 education session	NRS **-0.60 (−0.90, −0.30)**	QuickDASH **-0.56 (−0.86, −0.27)**

PEDro = Physiotherapy Evidence Database score; BMI = body mass index; SMD = Standardized Mean Difference; ACR = American College of Rheumatology; KL = Kellgren & Lawrence; OA = osteoarthritis; W = weight; H = height; f/u = follow-up; s = seconds; y = years; KOOS=Knee injury and Osteoarthritis Outcomes Score; ADL = function in activities of daily living; NRS = Numeric Pain Rating Scale; WOMAC = Western Ontario McMaster Osteoarthritis Questionnaire; Δ= change; NR = not reported
^(n) = PEDro scores available for original/related primary publication
*sample size analyzed immediately post-treatment (e.g., for intention-to-treat studies, it is the same as the number randomized);
**SMD, negative values indicate more favorable outcome (less pain, higher function) than comparison group
Bold = p < 0.05

Osteoarthritis and Cartilage

results are negative for exercise when compared to unblinded, inactive controls. The authors followed up with another recent editorial in which they estimated that regression to the mean might be as high as 1 point on a 0–10 point numeric rating scale for pain.[84] A couple of papers this year explicitly acknowledged contextual effects like regression to the mean to assist readers with interpreting study results.[37,69] Other researchers are also stepping forward to call on the scientific community to adopt a higher level of self-scrutiny in exercise trial design and interpretation.[85,86]

In light of the lack of highly effective treatments for managing OA in general, it is critical that further investigation into how treatments confer their effects in OA be undertaken, as well as further investigation into who might benefit most from which treatments. A systematic review of mediation analyses in OA interventions was published this year.[87] This study identified body weight, systemic inflammation, self-efficacy, and knee muscle strength as potential mediators of various treatments. However, these findings were primarily based on single studies. Clinical trials should be designed in anticipation of performing mediation analyses to ensure the correct variables are collected at the correct times to facilitate these analyses. Along with better understanding the 'how' of treatments, we also need to better understand which patient subgroups are most likely to benefit from which treatments. Clinical trials in isolation are substantially underpowered to perform moderation analyses. Meta-analyses of aggregate or individual participant data are therefore required to identify baseline characteristics that will predict better outcomes, something that is being undertaken by initiatives such as the OA Trial Bank.[85,86] Achieving this also requires consistent data collection and reporting, both of which require concerted collaboration from within the scientific community. High-quality mediation and moderation analyses, along with other mechanistic studies, will contribute to better understanding the mechanisms underpinning treatment effects, and thus developing more effective interventions.

Implementing guideline care in the real world

In a clinical care setting, interviews of individuals up to six years after receiving a surgical consultation for knee OA revealed that only one in five individuals had used guideline care to manage their OA.[88] This was in contrast to two in five who had used non-guideline care. This study highlights an implementation gap between evidence-based guideline recommendations and what is being recommended or utilized in real-world settings.

Critical appraisals of clinical practice guidelines suggest that one possible reason for the lack of successful implementation of guideline care is the low scores in the "Applicability" domain of most guidelines.[11] This suggests that most guidelines are not adequately considering or addressing how to implement guideline care into clinical or community settings. Other possible reasons for inadequate implementation could relate to clinician-specific or patient-specific factors. For example, Knoop et al. followed up their randomized clinical trial of stratified OA care with a qualitative study.[89] Physiotherapists interviewed reported feeling inadequately prepared to treat obesity, and felt that collaboration with dieticians was inadequate. Patients, on the other hand, reported issues of motivation to perform unsupervised exercises at home. Successful uptake of guideline care into clinical and community settings will likely require a multifaceted approach to address: applicability of guideline care; contextual factors that vary across regional health care systems; issues of systemic inequities and access to care; unique support and training for clinicians; and further research into patient desires and other facilitators and barriers to adherence and lifestyle modification in general. Implementation experts should be included throughout the life of a project to assist with bridging the gaps between research and clinical uptake.

Limitations

A key limitation of the present study relates to our decision to include studies of sufficiently high quality based on a sample size calculation from a single publication. The decision to use this threshold is somewhat arbitrary, and may have resulted in not reporting results from publications that were otherwise well-designed, or including studies that were nonetheless underpowered for their specific research questions. The art of power calculations is a challenge. For example, researchers often use a within-group MIC to estimate whether a study is large enough to detect a meaningful between-group difference, even though these two constructs differ. Moreover, MICs themselves are highly varied due to their susceptibility to methodological quality[90]. It is recommended that this approach be avoided, though a more robust solution has not yet been widely agreed-upon.[91] Using the minimal threshold of 90 per study arm – based on an expected difference rather than a MIC – may have been more prudent, but this would have limited our manuscript to just 16 studies.

Conclusions

Rehabilitation research in OA continues to be primarily focused on the knee joint. Most studies this year were not adequately powered to draw conclusions regarding the efficacy of treatments on pain, and inadequate attention is being given to better understanding mechanisms of treatment effect (e.g. using mediation analyses) or identification of subgroups that may be more likely to respond to certain treatments (e.g. moderation analyses). Although comparison to unblinded no or minimal intervention groups may no longer be recommended in exercise trials, further consideration of ideal control groups in this area is still needed in order to adequately address contextual effects like placebo and regression to the mean.

Funding

There was no funding for this review.

Declaration of Competing Interest

EM Macri received travel support from Osteoarthritis Research Society International (OARSI) to present the findings of this study at the OARSI World Congress in Denver, USA in March 2023. Authors declare no other competing interests.

Acknowledgements

We thank Wichor Bramer, health science librarian at Erasmus MC, for assisting us with developing our search terms and managing our search. We also thank researchers and clinicians from the Boston Musculoskeletal Clinical Research Collaboratory (Boston MCRC) Research Accelerator, for their critical feedback of our work (Research Accelerator is supported by a National Institutes of Health Core Center for Clinical Research grant (P30 AR072571).

Author contributions

All authors were involved in study design, interpretation of results, editing of manuscript and approving the final manuscript for submission. EMM, RWS, and JJS were involved in the search for eligible publications. EMM and JJS were involved in data extraction and analysis. EMM drafted the manuscript.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.joca.2023.08.011.

References

1. Bannuru RR, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra SMA, *et al.* OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthr Cartil 2019;27:1578–89. https://doi.org/10.1016/j.joca.2019.06.011
2. Brophy RH, Fillingham YA. AAOS clinical practice guideline summary: management of osteoarthritis of the knee (nonarthroplasty). J Am Acad Orthop Surg 2022;30:e721–9. https://doi.org/10.5435/JAAOS-D-21-01233
3. Wood G, Neilson J, Cottrell E, Hoole SP. Osteoarthritis in people over 16: diagnosis and management—updated summary of NICE guidance. BMJ 2023;380:e1–6. https://doi.org/10.1136/bmj.p24
4. Kloppenburg M, Kroon FPB, Blanco FJ, Doherty M, Dziedzic KS, Greibrokk E, *et al.* 2018 update of the EULAR recommendations for the management of hand osteoarthritis. Ann Rheum Dis 2019;78:16–24. https://doi.org/10.1136/annrheumdis-2018-213826
5. Fernandes L, Hagen KB, Bijlsma JWJ, Andreassen O, Christensen P, Conaghan PG, *et al.* EULAR recommendations for the nonpharmacological core management of hip and knee osteoarthritis. Ann Rheum Dis 2013;72:1125–35. https://doi.org/10.1136/annrheumdis-2012-202745
6. American Physical Therapy Association. Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guidline. Third ed. American Physical Therapy Association; 2021.
7. Krishnamurthy A, Lang AE, Pangarkar S, Edison J, Cody J, Sall J. Synopsis of the 2020 US Department of Veterans Affairs/US Department of Defense Clinical Practice Guideline: the non-surgical management of hip and knee osteoarthritis. Mayo Clin Proc 2021;96:2435–47. https://doi.org/10.1016/j.mayocp.2021.03.017
8. Royal Australian College of General Practitioners T. Guideline for the management of knee and hip osteoarthritis: technical document. RACGP, 2018. Vol. 2023: The Royal Australian College of General Practitioners; 2018.
9. Bruyère O, Honvo G, Veronese N, Arden NK, Branco J, Curtis EM, *et al.* An updated algorithm recommendation for the management of knee osteoarthritis from the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). Semin Arthritis Rheum 2019;49:337–50. https://doi.org/10.1016/j.semarthrit.2019.04.008
10. Lim YZ, Wong J, Hussain M, Estee MM, Zolio L, Page MJ, *et al.* Recommendations for weight management in osteoarthritis: a systematic review of clinical practice guidelines. Osteoarthr Cartil Open 2022;4:e1–20. https://doi.org/10.1016/j.ocarto.2022.100298
11. Gibbs A, Gray B, Wallis J, Kemp J, Taylor N, Hunter D, *et al.* Appraisal of clinical practice guidelines and recommendations for the management of hip and knee osteoarthritis: a systematic review. J Sci Med Sport 2022;25:S71–2. https://doi.org/10.1016/j.jsams.2022.09.088
12. Bichsel D, Liechti FD, Schlapbach JM, Wertli MM. Cross-sectional analysis of recommendations for the treatment of hip and knee osteoarthritis in clinical guidelines. Arch Phys Med Rehabil 2022;103:559–569. e5. https://doi.org/10.1016/j.apmr.2021.07.801
13. Sabha M, Hochberg MC. Non-surgical management of hip and knee osteoarthritis; comparison of ACR/AF and OARSI 2019 and VA/DoD 2020 guidelines. Osteoarthr Cartil Open 2022;4, 100232. https://doi.org/10.1016/j.ocarto.2021.100232
14. Waters P, Anderson R, Anderson JM, Scott J, Detweiler B, Streck S, *et al.* Analysis of the evidence underpinning the American Academy of Orthopedic Surgeons Knee Osteoarthritis Clinical Practice Guidelines. Sports Health 2023;15:11–25. https://doi.org/10.1177/19417381221112674
15. Zhang L, Wang Y, Ye T, Hu Y, Wang S, Qian T, *et al.* Quality of clinical practice guidelines relevant to rehabilitation of knee osteoarthritis: a systematic review. Clin Rehabil 2022;37:986–1008. https://doi.org/10.1177/02692155221144892
16. Conley B, Bunzli S, Bullen J, O'Brien P, Persaud J, Gunatillake T, *et al.* What are the core recommendations for osteoarthritis care? A systematic review of clinical practice guidelines. Arthritis Care Res 2023;75:1897–907. https://doi.org/10.1002/acr.25101
17. Overton C, Nelson AE, Neogi T. Osteoarthritis treatment guidelines from six professional societies: similarities and differences. Rheum Dis Clin 2022;48:637–57. https://doi.org/10.1016/j.rdc.2022.03.009
18. Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, *et al.* 2019 American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. Arthritis Rheumatol 2020;72:220–33. https://doi.org/10.1002/art.41142
19. Teirlinck CH, Verhagen AP, van Ravesteyn LM, Reijneveld-van de Vendel EAE, Runhaar J, van Middelkoop M, *et al.* Effect of exercise therapy in patients with hip osteoarthritis: a systematic review and cumulative meta-analysis. Osteoarthr Cartil Open 2023;5, 100338. https://doi.org/10.1016/j.ocarto.2023.100338
20. Verhagen AP, Ferreira M, Reijneveld-van de Vendel EAE, Teirlinck CH, Runhaar J, van Middelkoop M, *et al.* Do we need another trial on exercise in patients with knee osteoarthritis?: No new trials on exercise in knee OA. Osteoarthr Cartil 2019;27:1266–9. https://doi.org/10.1016/j.joca.2019.04.020
21. Paterson KL, Bennell KL, Metcalf BR, Campbell PK, McManus F, Lamb KE, *et al.* Effect of motion control versus neutral walking footwear on pain associated with lateral tibiofemoral joint osteoarthritis: a comparative effectiveness randomised clinical trial. BMJ Open 2022;12, e061627. https://doi.org/10.1136/bmjopen-2022-061627
22. Bennell KL, Schwartz S, Teo PL, Hawkins S, Mackenzie D, McManus F, *et al.* Effectiveness of an unsupervised online yoga program on pain and function in people with knee osteoarthritis: a randomized clinical trial. Ann Intern Med 2022;175:1345–55.
23. Physiotherapy Evidence Database. PEDro. vol. 2023.
24. Cashin AG, McAuley JH. Clinimetrics: Physiotherapy Evidence Database (PEDro) scale. J Physiother 2020;66:59. https://doi.org/10.1016/j.jphys.2019.08.005
25. Juhl C, Lund H, Roos EM, Zhang W, Christensen R. A hierarchy of patient-reported outcomes for meta-analysis of knee osteoarthritis trials: empirical evidence from a survey of high impact journals. Arthritis 2012:2012. https://doi.org/10.1155/2012/136245
26. Johnston BCPD, Devji T, Maxwell LJ, Bingham III CO, Beaton D, Boers M, *et al.* Patient-reported outcomes. In: Higgins JPTTJ, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editors. Cochrane handbook for systematic reviews of interventions version 6.3 (updated February 2022). Cochrane; 2022.
27. Cohen J. Statistical power analysis for the behavioral sciences. Hillsdale, NJ: Lawrence Earlbaum Associates; 1988. p. 6–20.
28. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. https://doi.org/10.1016/j.ijsu.2021.105906
29. Bennell KL, Lawford BJ, Keating C, Brown C, Kasza J, Mackenzie D, *et al.* Comparing video-based, telehealth-delivered exercise and weight loss programs with online education on outcomes of knee osteoarthritis: a randomized trial. Ann Intern Med 2022;175:198–209. https://doi.org/10.7326/M21-2388
30. Harris A, Hinman RS, Lawford BJ, Egerton T, Keating C, Brown C, *et al.* Cost effectiveness of telehealth-delivered exercise and

dietary weight loss programs for knee osteoarthritis within a 12-month randomised trial. Arthritis Care Res 2022;75:1311–9. https://doi.org/10.1002/acr.25022

31. Hunter DJ, Bowden JL, Hinman RS, Egerton T, Briggs AM, Bunker SJ, *et al*. Effectiveness of a new service delivery model for management of knee osteoarthritis in primary care: a cluster randomised controlled trial. Arthritis Care Res 2022;75:1320–32. https://doi.org/10.1002/acr.25037
32. Jönsson T, Dell'Isola A, Lohmander LS, Wagner P, Cronström A. Comparison of face-to-face vs digital delivery of an osteoarthritis treatment program for hip or knee osteoarthritis. JAMA Network Open 2022;5:e1–12. https://doi.org/10.1001/jamanetworkopen.2022.40126
33. Kaufman BG, Allen KD, Coffman CJ, Woolson S, Caves K, Hall K, *et al*. Cost and quality of life outcomes of the STepped exercise program for patients with knee osteoarthritis trial. Value Health 2022;25:614–21.
34. Knoop J, Dekker J, van Dongen JM, van der Leeden M, de Rooij M, Peter WF, *et al*. Stratified exercise therapy does not improve outcomes compared with usual exercise therapy in people with knee osteoarthritis (OCTOPuS study): a cluster randomised trial. J Physiother 2022;68:182–90. https://doi.org/10.1016/j.jphys.2022.06.005
35. Knoop J, Esser J, Dekker J, de Joode JW, Ostelo RWJG, van Dongen JM. No evidence for stratified exercise therapy being cost-effective compared to usual exercise therapy in patients with knee osteoarthritis: economic evaluation alongside cluster randomized controlled trial. Braz J Phys Ther 2023;27, 100469. https://doi.org/10.1016/j.bjpt.2022.100469
36. Liu J, Li Y, Li L, Luo X, Li N, Yang X, *et al*. Effects of acupuncture at acupoints with lower versus higher pain threshold for knee osteoarthritis: a multicenter randomized controlled trial. Chin Med 2022;17:1–12.
37. Messier SP, Beavers DP, Queen K, Mihalko SL, Miller GD, Losina E, *et al*. Effect of diet and exercise on knee pain in patients with osteoarthritis and overweight or obesity: a randomized clinical trial. JAMA 2022;328:2242–51. https://doi.org/10.1001/jama.2022.21893
38. Reichenbach S, Jüni P, Hincapié CA, Schneider C, Meli DN, Schürch R, *et al*. Effect of transcutaneous electrical nerve stimulation (TENS) on knee pain and physical function in patients with symptomatic knee osteoarthritis: the ETRELKA randomized clinical trial. Osteoarthr Cartil 2022;30:426–35. https://doi.org/10.1016/j.joca.2021.10.015
39. Coffman CJ, Arbeeva L, Schwartz TA, Callahan LF, Golightly YM, Goode AP, *et al*. Application of heterogeneity of treatment-effects methods: exploratory analyses of a trial of exercise-based interventions for knee osteoarthritis. Arthritis Care Res 2022;74:1359–68. https://doi.org/10.1002/acr.24564
40. Noorduyn JCA, van de Graaf VA, Willigenburg NW, Scholten-Peeters GGM, Kret EJ, van Dijk RA, *et al*. Effect of physical therapy vs arthroscopic partial meniscectomy in people with degenerative meniscal tears: five-year follow-up of the ESCAPE randomized clinical trial. JAMA Network Open 2022;5:e1–15. https://doi.org/10.1001/jamanetworkopen.2022.20394
41. Roesel I, Krauss I, Martus P, Steinhilber B, Mueller G. Comparison of a group-/home-based and a weight-machine-based exercise training for patients with hip or knee osteoarthritis—a secondary analysis of two trial interventions in a real-world context. Int J Environ Res Public Health 2022;19:17088. https://doi.org/10.3390/ijerph192417088
42. Henriksen M, Christensen R, Kristensen LE, Bliddal H, Bartholdy C, Boesen M, *et al*. Exercise and education versus intra-articular saline for knee osteoarthritis: a 1-year follow-up of a randomized trial. Osteoarthr Cartil 2023;5:627–35. https://doi.org/10.1016/j.joca.2022.12.011
43. Henriksen M, Nielsen SM, Christensen R, Kristensen LE, Bliddal H, Bartholdy C, *et al*. Who are likely to benefit from the good life with osteoarthritis in Denmark (GLAD) exercise and education program? An effect modifier analysis of a randomised controlled trial. Osteoarthr Cartil 2023;31:106–14. https://doi.org/10.1016/j.joca.2022.09.001
44. Pietsch A, Schroeder J, Dalichau S, Reer R, Engel D, Wahl-Wachendorf A, *et al*. Acute effects of an exercise based multimodal in-patient rehabilitation protocol in male knee osteoarthritis patients and the two years follow-up sustainability. Work 2023;75:1–11. https://doi.org/10.3233/WOR-205264
45. Torstensen TA, Østerås H, LoMartire R, Rugelbak GM, Grooten WJA, Äng BO. High-versus low-dose exercise therapy for knee osteoarthritis: a randomized controlled multicenter trial. Ann Intern Med 2023;176:154–65. https://doi.org/10.7326/M22-2348
46. Tveter AT, Østerås N, Nossum R, Eide REM, Klokkeide Å, Matre KH, *et al*. Short-term effects of occupational therapy on hand function and pain in patients with carpometacarpal osteoarthritis: secondary analyses from a randomized controlled trial. Arthritis Care Res 2022;74:955–64. https://doi.org/10.1002/acr.24543
47. Aree-Ue S, Roopsawang I, Saraboon Y, Youngcharoen P, Belza B, Kawinwonggowit V. A comprehensive health education plus monitoring support program for older adults with knee osteoarthritis coexisting with overweight and type 2 diabetes. Int J Nurs Sci 2022;9:512–20. https://doi.org/10.1016/j.ijnss.2022.08.002
48. Cagnin A, Choinière M, Bureau NJ, Durand M, Mezghani N, Gaudreault N, *et al*. Targeted exercises can improve biomechanical markers in individuals with knee osteoarthritis: a secondary analysis from a cluster randomized controlled trial. Knee 2023;40:122–34. https://doi.org/10.1016/j.knee.2022.10.008
49. de Zwart AH, Dekker J, Roorda LD, van der Esch M, Lips P, van Schoor NM, *et al*. High-intensity versus low-intensity resistance training in patients with knee osteoarthritis: a randomized controlled trial. Clin Rehabil 2022;36:952–67. https://doi.org/10.1177/02692155211073039
50. Thudium CS, Engstrøm A, Bay-Jensen A-C, Frederiksen P, Jansen N, De Zwart A, *et al*. Cartilage tissue turnover increases with high-compared to low-intensity resistance training in patients with knee OA. Arthritis Res Ther 2023;25:1–8. https://doi.org/10.1186/s13075-023-03000-2
51. Husted RS, Troelsen A, Husted H, Grønfeldt BM, Thorborg K, Kallemose T, *et al*. Knee-extensor strength, symptoms, and need for surgery after two, four, or six exercise sessions/week using a home-based one-exercise program: a randomized dose–response trial of knee-extensor resistance exercise in patients eligible for knee replacement (the QUADX-1 trial). Osteoarthr Cartil 2022;30:973–86. https://doi.org/10.1016/j.joca.2022.04.001
52. Heikkinen R, Waller B, Munukka M, Multanen J, Heinonen A, Karvanen J. Impact or no impact for women with mild knee osteoarthritis: a bayesian meta-analysis of two randomized controlled trials with contrasting interventions. Arthritis Care Res 2022;74:1133–41. https://doi.org/10.1002/acr.24553
53. Robson E, Kamper SJ, Lee H, Palazzi K, O'Brien KM, Williams A, *et al*. Compliance with telephone-based lifestyle weight loss programs improves low back pain but not knee pain outcomes: complier average causal effects analyses of 2 randomised trials. Pain 2022;163, e862. https://doi.org/10.1097/j.pain.0000000000002506
54. Cagnin A, Choinière M, Bureau NJ, Durand M, Mezghani N, Gaudreault N, *et al*. A multi-arm cluster randomized clinical trial of the use of knee kinesiography in the management of osteoarthritis patients in a primary care setting. Postgrad Med 2020;132:91–101. https://doi.org/10.1080/00325481.2019.1665457

55. Bandak E, Christensen R, Overgaard A, Kristensen L, Ellegaard K, Guldberg-Møller J, *et al*. Exercise and education versus saline injections for knee osteoarthritis: a randomised controlled equivalence trial. Ann Rheum Dis 2022;81:537–43. https://doi.org/10.1136/annrheumdis-2021-221129
56. O'Brien KM, Wiggers J, Williams A, Campbell E, Hodder RK, Wolfenden L, *et al*. Telephone-based weight loss support for patients with knee osteoarthritis: a pragmatic randomised controlled trial. Osteoarthr Cartil 2018;26:485–94. https://doi.org/10.1016/j.joca.2018.01.003
57. Williams A, Wiggers J, O'Brien KM, Wolfenden L, Yoong SL, Hodder RK, *et al*. Effectiveness of a healthy lifestyle intervention for chronic low back pain: a randomised controlled trial. Pain 2018;159: 1137–46. https://doi.org/10.1097/j.pain.0000000000001198
58. Allen KD, Woolson S, Hoenig HM, Bongiorni D, Byrd J, Caves K, *et al*. Stepped exercise program for patients with knee osteoarthritis: a randomized controlled trial. Ann Intern Med 2021;174:298–307. https://doi.org/10.7326/M20-4447
59. Nero H, Dahlberg J, Dahlberg LE. Joint academy – a six-week online treatment program for osteoarthritis. Osteoarthr Cartil 2018;26:S315. https://doi.org/10.1016/j.joca.2018.02.632
60. Thorstensson CA, Garellick G, Rystedt H, Dahlberg LE. Better management of patients with osteoarthritis: development and nationwide implementation of an evidence-based supported osteoarthritis self-management programme. Musculoskelet Care 2015;13:67–75. https://doi.org/10.1002/msc.1085
61. Krauss I, Mueller G, Haupt G, Steinhilber B, Janssen P, Jentner N, *et al*. Effectiveness and efficiency of an 11-week exercise intervention for patients with hip or knee osteoarthritis: a protocol for a controlled study in the context of health services research. BMC Public Health 2016;16:1–16. https://doi.org/10.1186/s12889-016-3030-0
62. Krauss I, Müller G, Steinhilber B, Haupt G, Janssen P, Martus P. Effectiveness and efficiency of different weight machine-based strength training programmes for patients with hip or knee osteoarthritis: a protocol for a quasi-experimental controlled study in the context of health services research. BMJ Open Sport Exerc Med 2017;3, e000291. https://doi.org/10.1136/bmjsem-2017-000291
63. Şah V. The short-term efficacy of large-focused and controlled-unfocused (radial) extracorporeal shock wave therapies in the treatment of hip osteoarthritis. J Pers Med 2022;13:48. https://doi.org/10.3390/jpm13010048
64. Martorella G, Mathis K, Miao H, Wang D, Park L, Ahn H. Self-administered transcranial direct current stimulation for pain in older adults with knee osteoarthritis: a randomized controlled study. Brain Stimul 2022;15:902–9. https://doi.org/10.1016/j.brs.2022.06.003
65. Martorella G, Mathis K, Miao H, Wang D, Park L, Ahn H. Efficacy of home-based transcranial direct current stimulation on experimental pain sensitivity in older adults with knee osteoarthritis: a randomized, sham-controlled clinical trial. J Clin Med 2022;11:5209. https://doi.org/10.3390/jcm11175209
66. Sawitzke AD, Jackson CG, Carlson K, Bizien MD, Leiner M, Reda DJ, *et al*. Effect of pulsed low-intensity ultrasonography on symptom relief and tibiofemoral articular cartilage thickness among veterans affairs enrollees with knee osteoarthritis: a randomized clinical trial. JAMA Network Open 2022;5:e1–14. https://doi.org/10.1001/jamanetworkopen.2022.0632
67. Sax OC, Gesheff MG, Mahajan A, Patel N, Andrews T-J, Jreisat A, *et al*. A novel mobile app-based neuromuscular electrical stimulation therapy for improvement of knee pain, stiffness, and function in knee osteoarthritis: a randomized trial. Arthroplast Today 2022;15:125–31. https://doi.org/10.1016/j.artd.2022.03.007
68. Jia L, Li D, Wei X, Chen J, Zuo D, Chen W. Efficacy and safety of focused low-intensity pulsed ultrasound versus pulsed shortwave diathermy on knee osteoarthritis: a randomized comparative trial. Sci Rep 2022;12:12792. https://doi.org/10.1038/s41598-022-17291-z
69. Larsen JB, Roos E, Laursen M, Holden S, Johansen MN, Rathleff MS, *et al*. Five-year follow-up of patients with knee osteoarthritis not eligible for total knee replacement: results from a randomised trial. BMJ Open 2022;12, e060169. https://doi.org/10.1136/bmjopen-2021-060169
70. Allen KD, Arbeeva L, Callahan LF, Golightly YM, Goode AP, Heiderscheit BC, *et al*. Physical therapy vs internet-based exercise training for patients with knee osteoarthritis: results of a randomized controlled trial. Osteoarthr Cartil 2018;26:383–96. https://doi.org/10.1016/j.joca.2017.12.008
71. Van De Graaf VA, Noorduyn JCA, Willigenburg NW, Butter IK, De Gast A, Mol BW, *et al*. Effect of early surgery vs physical therapy on knee function among patients with nonobstructive meniscal tears: the ESCAPE randomized clinical trial. JAMA 2018;320:1328–37. https://doi.org/10.1001/jama.2018.13308
72. Skou ST, Rasmussen S, Laursen MB, Rathleff MS, Arendt-Nielsen L, Simonsen O, *et al*. The efficacy of 12 weeks non-surgical treatment for patients not eligible for total knee replacement: a randomized controlled trial with 1-year follow-up. Osteoarthr Cartil 2015;23:1465–75. https://doi.org/10.1016/j.joca.2015.04.021
73. Zeng C, Yang T, Deng Zh, Yang Y, Zhang Y, Lei Gh. Electrical stimulation for pain relief in knee osteoarthritis: systematic review and network meta-analysis. Osteoarthr Cartil 2015;23:189–202. https://doi.org/10.1016/j.joca.2014.11.014
74. Wu Y, Zhu F, Chen W, Zhang M. Effects of transcutaneous electrical nerve stimulation (TENS) in people with knee osteoarthritis: A systematic review and meta-analysis. Clin Rehabil 2022;36:472–85. https://doi.org/10.1177/02692155211065636
75. Nascimento RMD, Cavalcanti RL, Souza CG, Chaves G, Macedo LB. Transcranial direct current stimulation combined with peripheral stimulation in chronic pain: a systematic review and meta-analysis. Expert Rev Med Devices 2023;20:121–40. https://doi.org/10.1080/17434440.2022.2039623
76. Chaturvedi R, Kulandaivelan S, Joshi S. Effectiveness of transcranial direct current stimulation on pain and function in knee osteoarthritis: a systematic review with meta-analysis based on PRiSMA guidelines. Physiother Q 2021;29:89–95. https://doi.org/10.5114/pq.2020.100282
77. Silva AC, Almeida VS, Veras PM, Carnaúba FRN, Filho JE, Garcia MAC, *et al*. Effect of extracorporeal shock wave therapy on pain and function in patients with knee osteoarthritis: a systematic review with meta-analysis and grade recommendations. Clin Rehabil 2023;37:760–73. https://doi.org/10.1177/026921552211460
78. Chen H, Wang Z, Zhang X, Sun M. Effects of low-intensity pulsed ultrasound on knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. Clin Rehabil 2022;36:1153–69.
79. Chen J, Liu A, Zhou Q, Yu W, Guo T, Jia Y, *et al*. Acupuncture for the treatment of knee osteoarthritis: an overview of systematic reviews. Int J Gen Med 2021:8481–94.
80. Giggins OM, Fullen BM, Coughlan GF. Neuromuscular electrical stimulation in the treatment of knee osteoarthritis: a systematic review and meta-analysis. Clin Rehabil 2012;26:867–81. https://doi.org/10.1177/0269215511431902
81. Tian H, Huang L, Sun M, Xu G, He J, Zhou Z, *et al*. Acupuncture for knee osteoarthritis: a systematic review of randomized clinical trials with meta-analyses and trial sequential analyses. BioMed Res Int 2022;2022:e1–15. https://doi.org/10.1155/2022/6561633

82. Englund M, Turkiewicz A. The emperor's new clothes? Osteoarthr Cartil 2023;31:549–51. https://doi.org/10.1016/j.joca.2023.02.001
83. Messier SP, Mihalko SL, Beavers DP, Nicklas BJ, DeVita P, Carr JJ, *et al.* Effect of high-intensity strength training on knee pain and knee joint compressive forces among adults with knee osteoarthritis: the START randomized clinical trial. JAMA 2021;325:646–57. https://doi.org/10.1001/jama.2021.0411
84. Englund M, Turkiewicz A. Pain in clinical trials for knee osteoarthritis: estimation of regression to the mean. Lancet Rheumatol 2023;5:e309–11. https://doi.org/10.1016/S2665-9913(23)00090-5
85. Hunter DJ, Hall M. Time to revisit the therapeutic benefits of exercise for osteoarthritis. Lancet Rheumatol 2023;7:e365–7. https://doi.org/10.1016/S2665-9913(23)00135-2
86. Holden MA, Hattle M, Runhaar J, Riley RD, Healey EL, Quicke J, *et al.* Moderators of the effect of therapeutic exercise for knee and hip osteoarthritis: a systematic review and individual participant data meta-analysis. Lancet Rheumatol 2023;5:e386–400. https://doi.org/10.1016/S2665-9913(23)00122-4
87. Lima YL, Lee H, Klyne DM, Dobson FL, Hinman RS, Bennell KL, *et al.* How do nonsurgical interventions improve pain and physical function in people with osteoarthritis? A scoping review of mediation analysis studies. Arthritis Care Res 2023;75:467–81. https://doi.org/10.1002/acr.24983
88. Mazzei DR, Whittaker JL, Kania-Richmond A, Faris P, Wasylak T, Robert J, *et al.* Do people with knee osteoarthritis use guideline-consistent treatments after an orthopaedic surgeon recommends nonsurgical care? A cross-sectional survey with long-term follow-up. Osteoarthr Cartil Open 2022;4, 100256. https://doi.org/10.1016/j.ocarto.2022.100256
89. Knoop J, de Joode JW, Brandt H, Dekker J, Ostelo R. Patients' and clinicians' experiences with stratified exercise therapy in knee osteoarthritis: a qualitative study. BMC Musculoskelet Disord 2022;23:1–14. https://doi.org/10.1186/s12891-022-05496-2
90. Macri EM, Young JJ, Ingelsrud LH, Khan KM, Terluin B, Juhl CB, *et al.* Meaningful thresholds for patient-reported outcomes following interventions for anterior cruciate ligament tear or traumatic meniscus injury: a systematic review for the OPTIKNEE consensus. Br J Sports Med 2022;56:1432–44. https://doi.org/10.1136/bjsports-2022-105497
91. Cook JA, Julious SA, Sones W, Hampson LV, Hewitt C, Berlin JA, *et al.* DELTA2 guidance on choosing the target difference and undertaking and reporting the sample size calculation for a randomised controlled trial. BMJ 2018;363:k3750.