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What Prognostic Indicators and Treatment Mechanisms Exist for Efficacious Treatments in People With Patellofemoral Pain? A Secondary Meta-regression With an Updated Search

■ **OBJECTIVE:** To investigate the prognostic and mechanistic variables associated with efficacious treatments in people with patellofemoral pain (PFP).

■ **DESIGN:** Updated intervention systematic review with de novo meta-regression.

■ **LITERATURE SEARCH:** We searched MEDLINE, Web of Science, and Scopus from inception until October 2023 for randomized controlled trials (RCTs) involving people with PFP.

■ **STUDY SELECTION CRITERIA:** High-quality RCTs (scoring ≥7 on the PEDro scale) involving participants with PFP and at least 1 treatment arm involving an efficacious intervention.

■ **DATA SYNTHESIS:** We extracted homogenous pain and function data to calculate effect sizes to regress with baseline prognostic (eg, symptom duration) and mechanistic (eg, strength change) data.

■ **RESULTS:** Thirty-four high-quality RCTs involving 1526 people with PFP were included. For knee-targeted exercise, we identified symptom duration ($R^2 = 0.68$), older age ($R^2 = 0.31$), and low baseline knee extensor strength ($R^2 = 1.0$) as significant prognostic variables. For hip-and-knee–targeted exercise, we identified older age ($R^2 = 0.37$), greater mass ($R^2 = 0.28$), and greater baseline hip abduction torque ($R^2 = 1.0$) as significant prognostic variables. We also identified a significant mechanistic association between pain and increased knee extensor torque ($R^2 = 0.99$). For hip-targeted exercise, we identified lower height as a significant prognostic variable ($R^2 = 0.96$-0.99) and a significant mechanistic association between both pain and function and increased hip abduction ($R^2 = 0.93$-0.96) and hip external rotation ($R^2 = 0.96$-0.97) strength.

■ **CONCLUSIONS:** Prolonged symptom duration, older age, and greater mass are prognostic variables for people with PFP. Increasing hip and knee muscle strength may be mechanisms underpinning positive responses to exercise therapy. *JOSPT Open 2025;3(2):193-209. Epub 6 February 2025. doi:10.2519/josptopen.2025.0119*

■ **KEY WORDS:** *mechanisms, meta-regression, patellofemoral pain, prognosis*

Patellofemoral pain (PFP) is a common musculoskeletal condition experienced by people of variable levels of physical activity. The main symptom is knee pain at, around, or behind the patella aggravated by running, squatting, and stair ambulation.[60] PFP has a reported prevalence of 28.9% in active adolescents and 22.7% in the general population,[56] with over 50% reporting persistent pain 5 to 8 years postdiagnosis.[36] This persistent pain experience negatively impacts physical activity levels, health-related quality of life, and social engagement,[20] and is theoretically linked to an increased potential for developing knee osteoarthritis.[15]

We recently conducted a systematic review with meta-analysis that pooled data from all available high-quality randomized controlled trials (RCTs) published up to May 2022.[46] This meta-analysis identified that 6 nonsurgical treatments (knee-targeted exercise; the combination of hip-and-knee–targeted exercise, soft tissue stretching, patellar taping, and quadriceps muscle biofeedback; foot orthoses; lower quadrant manual therapy; hip-and-knee–targeted exercise; and knee-targeted exercise combined with perineural dextrose injection) had positive effects on pain and function at short term (ie, ≤3/12) in people with PFP.[46] These pooled data demonstrated interventions that are beneficial at a population level, but not who is most likely to respond or via which mechanisms.

Previous systematic reviews with meta-analysis[35,38] and observational studies[36] have reported that variables including older age, higher baseline pain and poorer function, and prolonged symptom duration are associated with a poorer prognosis. The reviews were limited by poor quality methods, inappropriate control groups, and small sample sizes.[35,38] Lack et al[35] included only 15 low-quality cohort studies and no RCTs, leaving them unable to differentiate between predictors of outcome and prognostic factors. Matthews et al[38] identified that the prognostic studies included in their review typically explored too many prognostic variables relative to their sample size. A solution to this problem is to apply meta-regression techniques

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on data obtained in a systematic review using baseline prognostic indicators (eg, age) and intervention mechanisms (eg, a change in muscle strength) alongside treatment effect sizes. Compared to traditional meta-analysis, meta-regression provides valuable quantitative insight into the contribution of each indicator to the treatment effect. The field now has sufficient high-quality RCTs that report the required prognostic and mechanistic data to make this possible.

We aimed to conduct a meta-regression to investigate the prognostic indicators (ie, observational baseline data) and intervention mechanisms (ie, longitudinal change from baseline) from all available high-quality RCTs including at least 1 arm involving an intervention reported to be efficacious in our previous review.[46]

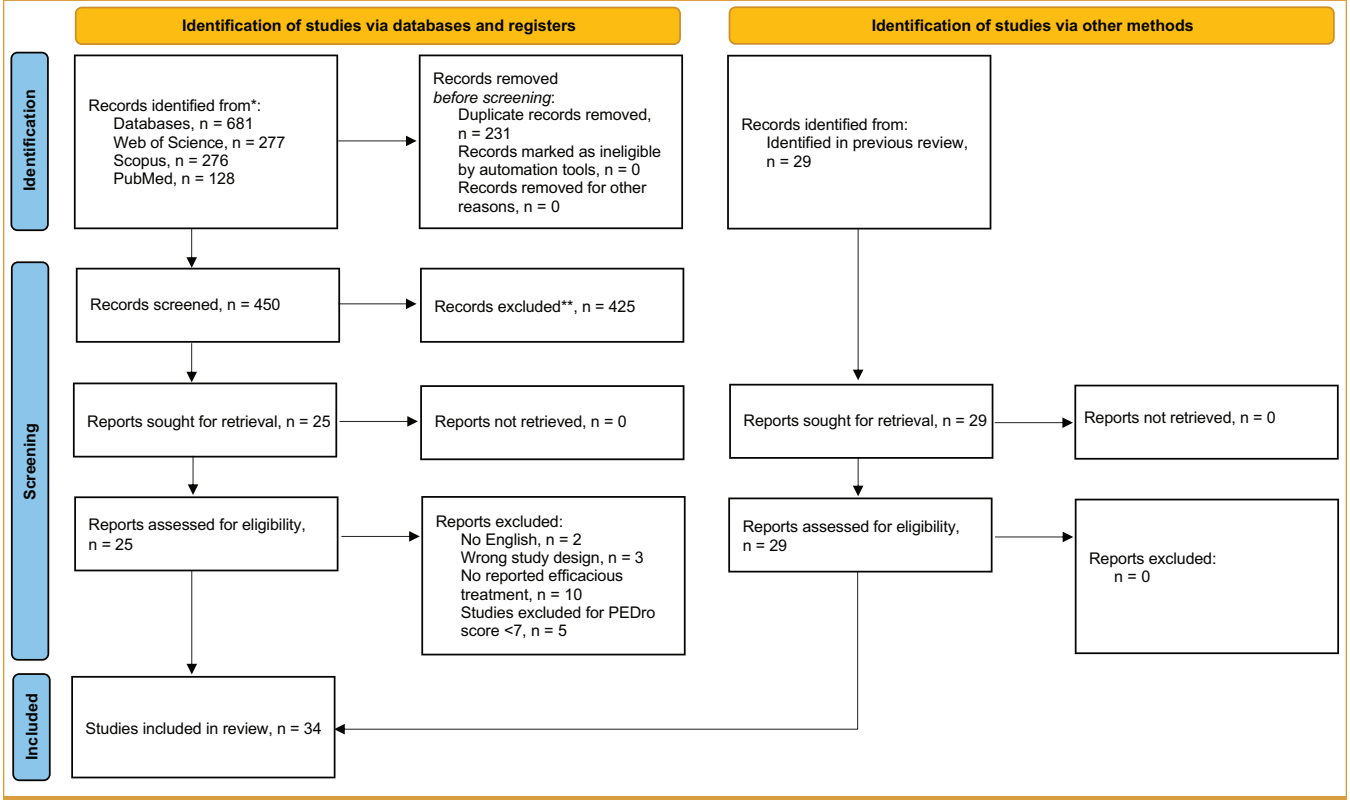
METHODS

We prospectively registered this systematic review with meta-regression with PROSPERO (CRD42023484049) and have 3 deviation from the original protocol: (1) postregistration, we included hip-targeted exercise therapy in our analyses as it was identified to be equivalent to knee-targeted exercise therapy (ie, an efficacious treatment) in our previous review;[46] (2) our protocol inaccurately refers to the use of 2 quality appraisal scales; and (3) we decided against attempting to use the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach as it does not align well with meta-regression outcomes. We have reported this systematic review with meta-regression per the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.[40]

Search Strategy

All high-quality RCTs from our previous review[46] were automatically eligible if they included at least 1 arm involving an intervention identified to have primary or secondary efficacy, superiority, or equivalence. We used the same search terms from our previous review,[46] originally duplicated from Barton et al,[2] with the English language and human participants as limitations: (patell* OR femoropat* OR anterior knee pain) AND (pain OR syndrome OR dysfunction) AND (clinical trial OR controlled trial OR random*). We searched the same 3 databases (MEDLINE, Web of Science, and Scopus) from May 2022 to October 2023 to identify new RCTs meeting our

FIGURE 1
Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.



eligibility criteria, with inception to May 2022 captured by our previous search.

Inclusion Criteria

One investigator (B.S.N.) exported all identified studies into Covidence (Veritas Health Innovation Ltd, Melbourne, Australia). We adapted the eligibility criteria from our previous review, again originally duplicated from Barton et al:[2] (1) RCTs involving adult participants aged >18 to 45 years, (2) participants with PFP defined as insidious onset symptoms aggravated by activities such as running, jumping, squatting, or stair ambulation, (3) RCTs investigating nonsurgical interventions, and (4) RCTs including at least 1 arm involving an intervention reported to have primary or secondary efficacy, superiority, or equivalence. RCTs including participants with traumatic onset of symptoms or symptoms commencing postsurgery or participants with concomitant pathology were ineligible.

Two investigators (F.D. and M.R.) reviewed all titles and abstracts independently to determine eligibility by consensus, reviewing full texts if necessary. A third investigator (B.S.N.) was available but not required to resolve discrepancies. Once all new eligible RCTs were identified, 2 investigators (F.D. and B.S.N.) reviewed them independently to determine if they contained at least 1 eligible treatment arm analogous to (1) knee-targeted exercise; (2) the combination of hip-and-knee–targeted exercise, soft tissue stretching, patellar taping, and quadriceps muscle biofeedback; (3) prefabricated foot orthoses; (4) lower quadrant manual therapy; (5) hip-and-knee–targeted exercise; (6) knee-targeted exercise combined with perineural dextrose injection; and (7) hip-targeted exercise. Eligible RCTs were retained for quality assessment.

PFP Diagnostic Criteria

All retained RCTs were appraised relative to the PFP diagnostic criteria described by Barton et al,[3] which considers adherence to specific inclusion and exclusion criteria. The score for RCTs included in our previous review was automatically recorded, and newly identified RCTs were screened by 2 independent reviewers (F.D. and B.S.N.) before agreeing a consensus score. A third investigator (A.B.J.) was available but not required to resolve discrepancies that could not be resolved by consensus.

Quality Assessment

We used the PEDro scale[37] to determine methodological quality as per our previous review.[46] Two investigators (F.D. and B.S.N.) applied the PEDro scale

TABLE 1
PEDRO Scores for the Retained High-Quality Randomized Controlled Trials

Study	A	B	C	D	E	F	G	H	I	J	Total
Previous Search (29 Trials)											
Baldon et al[1]	1	1	0	1	0	0	1	1	1	1	7
Behrangrad and Kamali[4]	1	1	1	1	1	0	1	0	1	1	8
Bolgla et al[5]	1	0	1	0	0	1	1	1	1	1	7
Celik et al[7]	1	0	1	1	0	0	1	1	1	1	7
Clark et al[8]	1	0	1	0	0	1	1	1	1	1	7
Collins et al[9]	1	1	1	0	0	1	1	1	1	1	8
Crossley et al[12]	1	1	1	1	0	1	1	1	1	1	9
Das et al[13]	1	0	1	1	0	1	1	0	1	1	7
Espí-López et al[16]	1	1	1	0	0	1	1	1	1	1	8
Fukuda et al[18]	1	1	1	0	0	1	1	1	1	1	8
Fukuda et al[17]	1	1	1	0	0	1	1	1	1	1	8
García-Triana et al[19]	1	1	1	0	0	1	1	0	1	1	7
Halabchi et al[21]	1	1	1	0	0	0	1	1	1	1	7
Hott et al[28]	1	1	0	0	0	1	1	1	1	1	7
Hott et al[29]	1	1	0	0	0	1	1	1	1	1	7
Ismail et al[30]	1	1	1	0	0	1	1	0	1	1	7
Matthews et al[39]	1	1	0	1	1	1	1	1	1	1	9
Mølgaard et al[41]	1	1	1	0	0	1	0	1	1	1	7
Motealleh et al[43]	1	1	1	0	0	1	1	0	1	1	7
Nakagawa et al[44]	1	1	1	1	0	1	1	0	1	1	8
Rasti et al[50]	1	1	1	1	0	1	1	0	1	1	8
Saad et al[52]	1	1	0	0	0	1	1	1	1	1	7
Sahin et al[53]	1	1	1	0	0	1	1	0	1	1	7
Song et al[57]	1	1	1	0	0	1	1	1	1	1	8
Van den Dolder and Roberts[59]	1	1	1	0	0	1	1	1	1	1	8
Wu et al[61]	1	1	1	0	0	1	1	1	1	1	8
Yañez-Álvarez et al[62]	1	0	1	0	0	1	1	1	1	1	7
Zago et al[64]	1	1	1	0	0	1	1	1	1	1	8
Zarei et al[65]	1	1	0	0	0	1	1	1	1	1	7
Updated Search (5 Trials)											
Hansen et al[22]	1	1	1	0	0	1	1	1	1	1	8
Kumar et al[34]	1	1	1	0	1	1	0	0	1	1	7
Pompeo et al[48]	1	1	1	0	1	1	1	1	1	1	9
Silva et al[55]	1	1	1	0	0	1	1	1	1	1	8
Zafarian et al[63]	1	0	1	1	0	1	1	0	1	1	7

Abbreviations: A, random allocation; B, concealed allocation; C, comparable groups at baseline; D, participant blinding; E, clinician blinding; F, outcome assessor blinding; G, >85% data collection; H, intention-to-treat analyses; I, between-group statistical comparisons; J, variability reported.

TABLE 2
Data Extraction From the Retained High-Quality Randomized Controlled Trials

Study	Sample Size (F:M) Age in years (mean ±) Height in cm (mean ±) Mass in kg (mean ±) BMI in kg/m^2 (mean ±) Symptom Duration in Months (mean ±)		Extracted Pain Outcome	Extracted Function Outcome	Extracted Mechanistic Variables	Treatment
	Group 1	Group 2				
Baldon et al[1]	16 (16:0) 21.3 ± 2.6 160 ± 10 58.3 ± 7.3 22.3 ± 2.5 27 ± NR	15 (15:0) 22.7 ± 3.2 166 ± 10 57.1 ± 8.2 20.6 ± 2.9 60 ± NR	W-VAS	LEFS	Kinematics (Hip FLEX, EXT, ADD, ABD; Knee ADD, ABD) Eccentric torque (Hip ABD, ADD, ER, IR; Knee EXT, FLEX)	Group 1: Knee exercise Group 2: Hip-and-knee exercise
Bolgla et al[5]	80 (51:29) 29.3 ± 0.9 171.2 ± 1.0 71.1 ± 1.7 NR NR	105 (73:32) 29.4 ± 0.7 170.0 ± 1.0 67.0 ± 1.3 NR NR	VAS	Kujala	Muscle strength (Hip ABD, EXT, ER; Knee EXT)	Group 1: Knee exercise Group 2: Hip exercise
Das et al[13]	14 (9:6) 32.7 ± 9.7 NR NR NR 7.7 ± 4.3	NR	VAS	Kujala	Surface EMG (MVC during Knee EXT)	Group 1: Knee exercise
Fukuda et al[18]	20 (20:0) 25.0 ± 6.0 164 ± 60 57.1 ± 7.3 NR NR	21 (21:0) 25.0 ± 7.0 162 ± 60 61.3 ± 8.1 NR NR	NPRS-AS	Kujala	NR	Group 1: Knee exercise Group 2: Hip-and-knee exercise
Fukuda et al[17]	24 (24:0) 23.0 ± 3.0 160 ± 30 61.5 ± 3.6 24.5 ± 3.0 21.0 ± 17.7 NR	25 (25:0) 22.0 ± 3.0 159 ± 10 60 ± 26 23.6 ± 2.7 23.2 + 19 NR	NPRS-DS	Kujala	NR	Group 1: Knee exercise Group 2: Hip-and-knee exercise
García-Triana et al[19]	25 (20:5) 53.5 ± 14.4 NR NR NR NR	NR	VAS	WOMAC (function)	NR	Group 1: Knee exercise

Hansen et al[22]	98 (64:34) 27.2 ± 6.3 172.4 ± 8.5 68.2 ± 12.4 22.8 ± 3.0 47.3 ± 49.4	100 (72:28) 27.2 ± 6.7 173.2 ± 10.7 67.6 + 13.0 22.4 ± 2.9 52.8 ± 54.1	VAS	KOOS-function	Isometric muscle strength (Hip ABD, ADD, EXT, FLEX, ER, IR; Knee EXT, FLEX)	Group 1: Knee exercise Group 2: Hip exercise
Halabchi et al[21]	30 (18:12) 29.3 ± 5.9 NR NR 21.6 ± 2.4 30.1 ± 22.4	30 (17:13) 30.1 ± 5.9 NR NR 24.3 ± 3.9 31.9 ± 21.2	VAS	Kujala	NR	Group 1: Knee exercise Group 2: Combined interventions
Hott et al[28]	37 (24:13) 28.5 ± 6.2 NR NR NR NR	39 (25:14) 27.8 ± 8.6 NR NR NR NR	U-VAS	Kujala	Isometric muscle strength (Hip ABD, ER; Knee EXT)	Group 1: Knee exercise
Hott et al[29]	37 (24:13) 28.5 ± 6.2 NR NR NR NR	NR	U-VAS	Kujala	Isometric muscle strength (Hip ABD, ER; Knee EXT)	Group 1: Knee exercise
Ismail et al[30]	16 (12:4) 21.2 ± 3.2 165.7 ± 5.3 66.6 ± 9.8 NR NR	16 (11:5) 20.8 ± 2.7 163.6 ± 8.5 64.5 ± 9.6 NR NR	VAS	Kujala	Concentric and eccentric torque (Hip ABD, ER)	Group 1: Knee exercise Group 2: Hip-and-knee exercise
Kumar et al[34]	30 (NR) 29.2 ± 1.2 161.2 ± 1.7 68.0 ± 1.3 26.7 ± 0.8 NR	NR	VAS	Kujala	Muscle CSA, fascicle length, and pennation angles (VM, VIM, VL, and RF)	Group 1: Knee exercise
Mølgaard et al[41]	20 (14:6) 29.5 ± NR 174 ± NR 75.1 ± NR 25.3 ± NR 70 ± NR	NR	VAS	Kujala	NR	Group 1: Knee exercise

(Table continues on next page.)

TABLE 2
Data Extraction From the Retained High-Quality Randomized Controlled Trials (continued)

Study	Sample Size (F:M) Age in years (mean ffl) Height in cm (mean ffl) Mass in kg (mean ffl) BMI in kg/m2 (mean ffl) Symptom Duration in Months (mean ffl)		Extracted Pain Outcome	Extracted Function Outcome	Extracted Mechanistic Variables	Treatment
	Group 1	Group 2				
Motealleh et al[43]	14 (14:0) 30.4 ± 6.1 159 ± 5 58.9 ± 7.9 23.2 ± 3.3 NR	14 (14:0) 28.4 ± 5.7 161 ± 6 58.5 ± 8.8 22.6 ± 3.0 NR	VAS	Kujala	NR	Group 1: Knee exercise Group 2: Hip-and-knee exercise
Nakagawa et al[44]	7 (NR) 23.6 ± 5.9 NR NR NR NR	7 (NR) 23.6 + 5.9 NR NR NR NR	W-VAS	NR	Eccentric torque (HIP ABD, ER; Knee EXT) Surface EMG (MVC GMED)	Group 1: Knee exercise Group 2: Hip-and-knee exercise
Saad et al[52]	10 (10:0) 23.2 ± 2.5 161 ± 7.0 56.3 ± 5.9 21.8 ± 1.7 NR	10 (10:0) 22.5 ± 1.1 159.0 ± 3.0 55.3 + 4.0 22.0 ± 2.0 NR	VAS	Kujala	Kinematics (dynamic knee valgus) Isometric muscle strength (Hip ABD, ADD, ER, IR, EXT, FLEX; Knee EXT, FLEX)	Group 1: Knee exercise Group 2: Hip exercise
Sahin et al[53]	25 (25:0) 35.0 ± 5.9 NR NR 26.4 ± 3.5 6 ± NR	25 (25:0) 33.3 ± 6.5 NR NR 25.5 ± 4.4 8 ± NR	VAS	Kujala	Peak torque (Hip ABD and ER)	Group 1: Knee exercise Group 2: Hip-and-knee exercise
Song et al[57]	30 (22:8) 40.2 ± 9.9 161.3 ± 8.4 60.1 ± 11.2 23.0 ± 3.0 38.3 ± 34.2	29 (21:8) 38.6 ± 10.8 162.3 ± 7.2 58.3 ± 9.0 22.2 ± 3.2 41.8 ± 36.1	W-VAS	Lysholm	Muscle morphology (VMO CSA)	Group 1: Knee exercise Group 2: Hip-and-knee exercise
Clark et al[8]	20 (8:12) 29.5 ± 6.2 NR NR 24.9 ± 4.2 NR	NR	VAS	WOMAC	Isometric muscle strength (Knee EXT)	Group 1: Hip-and-knee exercise

Celik et al[7]	13 (7:6) 41.5 ± 12.7 162.3 ± 8.4 66.3 ± 11 NR NR	15 (9:5) 39.1 ± 9.1 166.2 ± 6.4 75.1 ± 13.4 NR NR	NR	Kujala	Concentric peak torque (Knee EXT, FLEX)	Group 1: Knee exercise Group 2: Combined interventions
Espí-López et al[16]	30 (15:15) 29.7 ± 9.5 170 ± 10 68.9 ± 13.2 NR NR	NR	NPRS	KOOS-ADL	NR	Group 1: Hip-and-knee exercise
Pompeo et al[48]	25 (25:0) 28.7 ± 6.4 164 ± 6 60.7 ± 7.4 22.7 ± 2.5 NR	NR	VAS	Kujala	Kinematics (Dynamic Valgus Index) Isometric muscle strength (Hip ABD, EXT, ER; Knee EXT, FLEX; Ankle EV, IV)	Group 1: Hip-and-knee exercise
Rasti et al[50]	12 (12:0) 24.2 ± 5.2 177.5 ± 6.2 76.7 ± 5.7 24.3 ± 0.0 NR	NR	VAS	Kujala	Vertical jump; Flexibility; Agility	Group 1: Hip-and-knee exercise
Silva et al[55]	35 (35:0) 22.7 ± 3.1 163 ± 5.8 61.6 ± 10.8 NR NR	NR	VAS	ADLS	Kinematics (Lateral trunk FLEX; trunk FLEX; pelvic drop; Hip FLEX; Knee valgus, FLEX; Ankle DF) Isometric torque (Hip ER, ABD, EX; Knee EXT)	Group 1: Hip-and-knee exercise
Wu et al[61]	18 (9:9) 27.3 ± NR NR NR 21.7 ± NR NR	NR	VAS	Kujala	Surface EMG (GMED and VM, RMS and MF)	Group 1: Hip-and-knee exercise
Yañez-Álvarez et al[62]	25 (12:13) 52 ± 10.7 169 ± 9.3 82.2 ± 18.1 28.5 ± 4.7 NR	NR	VAS	Kujala	Joint ROM (Knee FLEX, EXT)	Group 1: Hip-and-knee exercise

(Table continues on next page.)

TABLE 2
Data Extraction From the Retained High-Quality Randomized Controlled Trials (continued)

Study	Sample Size (F:M) Age in years (mean ffl) Height in cm (mean ffl) Mass in kg (mean ffl) BMI in kg/m2 (mean ffl) Symptom Duration in Months (mean ffl)		Extracted Pain Outcome	Extracted Function Outcome	Extracted Mechanistic Variables	Treatment
	Group 1	Group 2				
Zarei et al[65]	20 (20:0) 25.7 ± 8.5 161 ± 7 55.7 ± 7.7 NR NR	NR	NPRS	Kujala	PPT	Group 1: Hip-and-knee exercise
Behrangrad and Kamali[4]	15 (12:3) 24.3 ± 1.9 168.3± 5.3 55± 8.2 19.4 ± 2.2 NR	NR	NRPS	Kujala	PPT	Group 1: Lower quadrant manual therapy
Van den Dolder and Roberts[59]	21 (17:4) 55 ± 11 NR NR NR 26 ± NR	NR	U-VAS	NR	Joint ROM (Knee FLEX, EXT)	Group 1: Lower quadrant manual therapy
Zago et al[64]	30 (18:12) 31.4 ± 7.2 171.6 ± 8.1 69.4 ± 5.1 24.1 ± 2.8 NR	NR	VAS	Lysholm	Kinematics (dynamic knee valgus) Kinetics (plantar pressures) Joint ROM (Hip EXT)	Group 1: Lower quadrant manual therapy
Zafarian et al[63]	13 (8:5) 29.8 ± 7.8 167.4 ± 9.8 67.5 ± 8.0 24.2 ± 3.4 NR	NR	NPRS	Kujala	Surface EMG (average amplitude and onset in GMED and VM)	Group 1: Lower quadrant manual therapy

Collins et al[9]	46 (25:21)	45 (29:16)	GROC		NR	Group 1: Foot orthoses
	27.9 ± 5.3	30.9 ± 5.8				Group 2: Combined interventions
	172.8 ± 9.1	170.9 + 8.4				
	78.5 ± 20.4	70.9 + 14.6				
	26.1 + 5.6	24.2 ± 4.7				
	42 ± NR	37 ± NR				
Matthews et al[39]	109 (81:28)	109 (70:39)	GROC		NR	Group 1: Hip exercise
	27.9 ± 6.0	28.3 ± 6.0				Group 2: Foot orthoses
	171.0 ± 9.4	171.4 + 9.8				
	72.5 ± 16.2	75.3 ± 16.9				
	24.7 ± 4.8	25.5 ± 4.9				
	55.4 ± 60.8	52.3 ± 61.9				
Crossley et al[12]	36 (23:13)	NR	U-VAS	Kujala	NR	Group 1: Combined interventions
	29.0 + 8.0					
	170.0 + 9.0					
	68.6 ± 13.7					
	23.5 ± 3.8					
	39.0 ± 43.0					

Abbreviations: ABD, abduction; ADD, adduction; ADL, activities of daily living; BMI, body mass index; CSA, cross-sectional area; EMG, electromyography; ER, external rotation; EXT, extension; F, female; FLEX, flexion; GMED, gluteus medius; GROC, global rating of change; IR, internal rotation; KOOS, knee injury and osteoarthritis outcome score; LEFS, lower extremity functional scale; M, male; MVC, maximal voluntary contraction; NPRS, numerical pain-rating scale; NPRS-AS, numerical pain-rating scale when ascending stairs; NPRS-DS, numerical pain-rating scale when descending stairs; NR, not reported; PPT, pain pressure threshold; RF, rectus femoris; ROM, range of movement; U-VAS, usual visual analogue scale; VAS, visual analogue scale; VAS-A, visual analogue scale during activity; VL, vastus lateralis; VM, vastus medialis; VMO, vastus medialis obliquus; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; W-VAS, worst visual analogue scale.

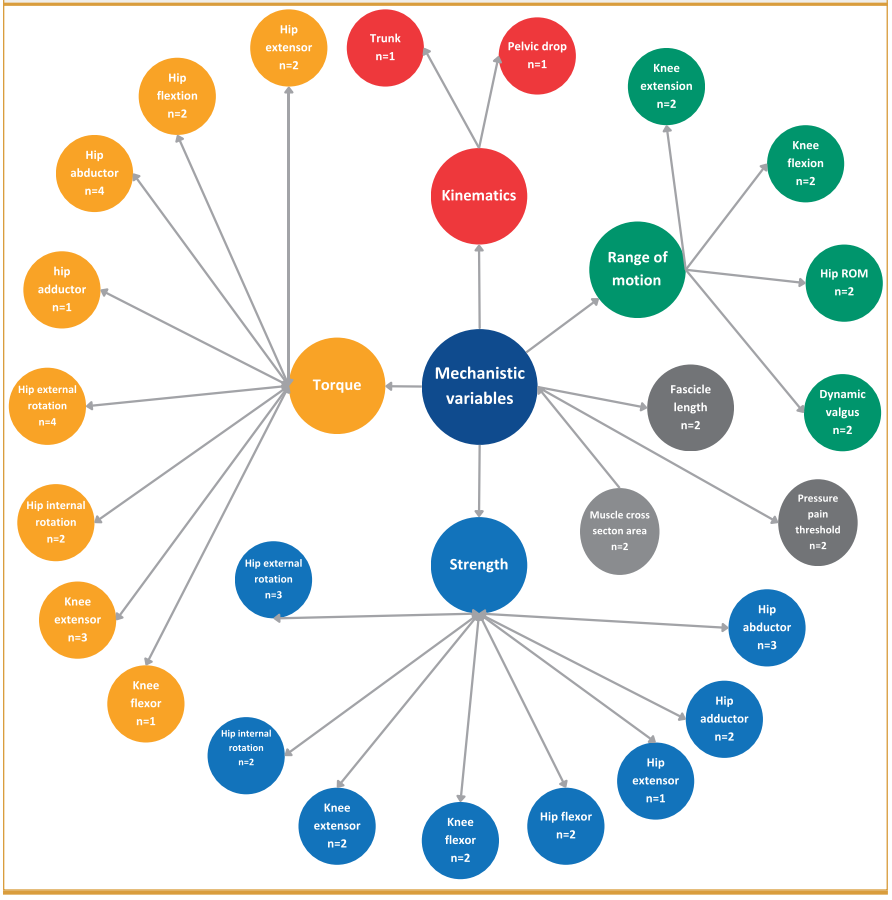
independently to all retained RCTs before achieving consensus on a total score. A third investigator (A.B.J.) was available but not required to resolve discrepancies that could not be resolved by consensus. To align with our previous review, scores of ≥7 reflected high quality[42] and only these RCTs were retained for meta-regression.

Data Extraction

One investigator (F.D.) extracted data from all RCTs retained for meta-regression, and the accuracy of data extraction was reviewed by a second investigator (B.S.N.). Data extracted included descriptive data (eg, lead author, publication year, interventions, sample size), baseline prognostic data (eg, participant sex, age, height, mass, body mass index [BMI], involved limb, symptom duration), and mechanistic data (eg, change in kinematics, kinetics, muscle function). Data that could be both prognostic (eg, baseline muscle strength) and mechanistic (eg, change in muscle strength postintervention) were extracted as such. We also extracted means (M) and standard deviations (SD) for pain (eg, numerical pain-rating scale) and function (eg, the Kujala scale) at baseline and follow-up to calculate an effect size ($[[M_1 - M_2] / [\sqrt{SD_1^2 + SD_1^2/2}]]$).[51]

As our previous review identified only short-term efficacy (≤3 months), this was the timeframe used for data extraction. Where RCTs presented more than 1 pain or function outcome, the outcome with the smallest within-group effect was extracted to minimize the potential for type I error as per our previous review. If no SD was reported, then the interquartile range or any other type of data was used to calculate SD according to the Cochrane Handbook.[26] Original authors were contacted a maximum of twice if data were missing or presented in a format that was inconsistent with our requirements.

FIGURE 2
Prevalence of mechanistic variables. Abbreviation: ROM, range of motion.



Meta-regression

Statistical analyses were conducted using R (Version 2023.09.0+463; R Core Team 2021). We performed random effects meta-regression to analyze the correlation between prognostic or mechanistic data and treatment effect sizes for pain and function outcomes. It is broadly accepted that between 8 and 25 data points are required for meta-regression.[31] We anticipated having limited ability to frequently pool homogeneous data from ≥8 RCTs and so set a threshold of ≥3 RCTs per regression adhering to the R programming language. The detailed code used for our meta-regressions is reported in **SUPPLEMENTAL FILE 1**. Mean baseline prognostic data were regressed with effect sizes for both pain and function outcomes, ensuring that prognostic data were all converted to the same unit of measurement. For mechanistic data, an effect size for change was regressed with effect sizes for both pain and function outcomes. An α level was set a priori at ≤.05. Correlation coefficients (adjusted R^2) were interpreted as per Schober et al,[54] categorized as negligible (0.00–0.09), weak (0.10–0.39), moderate (0.40–0.69), strong (0.70–0.89), and very strong (≥0.90).

RESULTS

Twenty-nine high-quality RCTs[1,4,5,7–9,12,13,16–19,21,28–30,39,41,43,44,50,52,53,57,59,61,62,64,65] from our previous review had at least 1 appropriate treatment arm. From the updated search, 681 studies were imported to Covidence. After removing duplicates and screening titles and abstracts followed by full texts against our inclusion criteria, 10 new RCTs[22,24,27,32–34,48,55,58,63] were eligible for quality assessment (**FIGURE 1**). After screening these 10 new RCTs using the PEDro scale, five[22,34,48,55,63] scored ≥7 and were retained for meta-regression (**TABLE 1**). PFP diagnostic criteria scores ranged from 1 to 7, and individual scores are detailed in **SUPPLEMENTAL FILE 2**. We included a total of 34 high-quality RCTs[1,4,5,7–9,12,13,16–19,21,22,28–30,34,39,41,43,44,48,50,52,53,55,57,59,61–65] for data extraction (**TABLE 2**). We received raw data from 4 out of 8 authors contacted. We were able to perform meta-regression for 5/7 efficacious treatments, with no prognostic or mechanistic data available from >3 RCTs for foot orthoses or knee-targeted exercise combined with perineural dextrose injection.

Baseline Prognostic Variables

Five unique prognostic variables were reported by at least 1 eligible RCT: 24 RCTs (70.6%) reported mass and BMI, 34 RCTs (100%) reported age, 26 RCTs (76.5%) reported height, and 14 RCTs (41.2%) reported symptom duration.

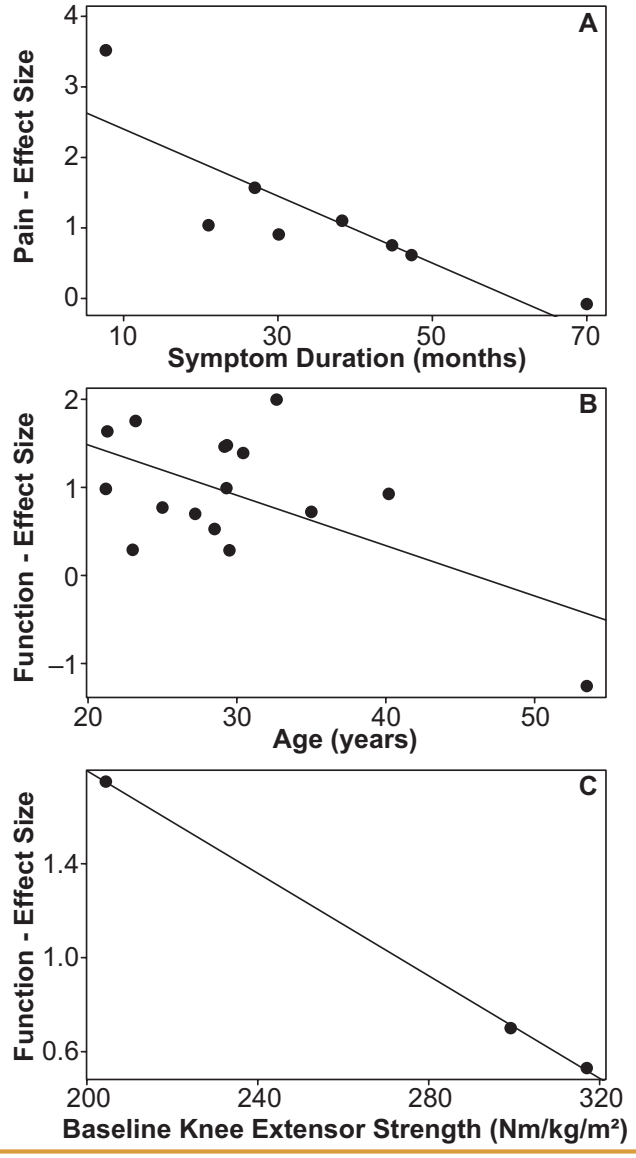
Mechanistic Variables

Twenty-six unique mechanistic variables were reported by at least 1 eligible RCT, which we categorized as strength, torque, kinematics, range of motion, morphology, and pain perception (**FIGURE 2**).

Sensitivity Analysis

Torque data reported by Nakagawa et al[44] were visually heterogeneous to torque data reported by other included RCTs. Nakagawa et al[44] reported their torque data in Nm/kg and did not report baseline BMI to allow us to normalize these data to the same unit as other torque data ($Nm/kg/m^2$). We therefore conducted a sensitivity analysis (**SUPPLEMENTAL FILE 3**) and identified no significant change in

FIGURE 3
Regression in knee-targeted exercise therapy. (A; left) Association between effect size for pain and prolonged symptom duration. (B; middle) Association between effect size for function and older age. (C; right) Association between effect size for function and low knee extensor strength.



outcome after removing data reported by Nakagawa et al,[44] so these data were therefore retained.

Relationship Between Pain, Function, and Baseline Prognostic Data for Knee-Targeted Exercise Therapy

Only significant associations are described in the text below. Nonsignificant associations are detailed in **SUPPLEMENTAL FILE 4**.

We identified a significant association between effect size for pain and prolonged symptom duration (8 RCTs,[1,13,17,21,22,28,41,57] moderate adjusted R^2= 0.68, P = .01; **FIGURE 3A**).

We identified a significant association between effect size for function and older age (17 RCTs,[1,5,13,17–19,21,22,28,30,34,41,43,52,53,57] weak adjusted R^2= 0.31, P = .02) and low knee extensor strength (3 RCTs,[22,28,52] very strong adjusted R^2= 1.0, P = .01; **FIGURE 3B-C**).

Relationship Between Pain, Function, and Baseline Prognostic Data for Hip-and-Knee–Targeted Exercise Therapy

We identified a significant association between effect size for function and older age (14 RCTs,[1,8,16–18,30,48,50,53,55,57,62,65] weak adjusted R^2= 0.37, P = .01), greater mass (12 RCTs,[1,7,16–18,30,43,48,55,57,62,65] weak adjusted R^2= 0.28, P = .05), and greater hip abduction torque (3 RCTs,[1,7,55] adjusted R^2= 1.0, P = .02; **FIGURE 4A-C**).

Relationship Between Pain, Function, and Mechanistic Data for Hip-and-Knee–Targeted Exercise Therapy

We identified a significant association between effect size for pain and increased knee extensor torque (3 RCTs,[1,44,55] very strong adjusted R^2= 0.99, P = .05; **FIGURE 4D**).

Relationship Between Pain, Function, and Baseline Prognostic Data for Hip-Targeted Exercise Therapy

We identified a significant association between effect size for pain and lower height (5 RCTs,[5,22,28,39,52] very strong adjusted R^2= 0.99, P = .00; **FIGURE 5A**).

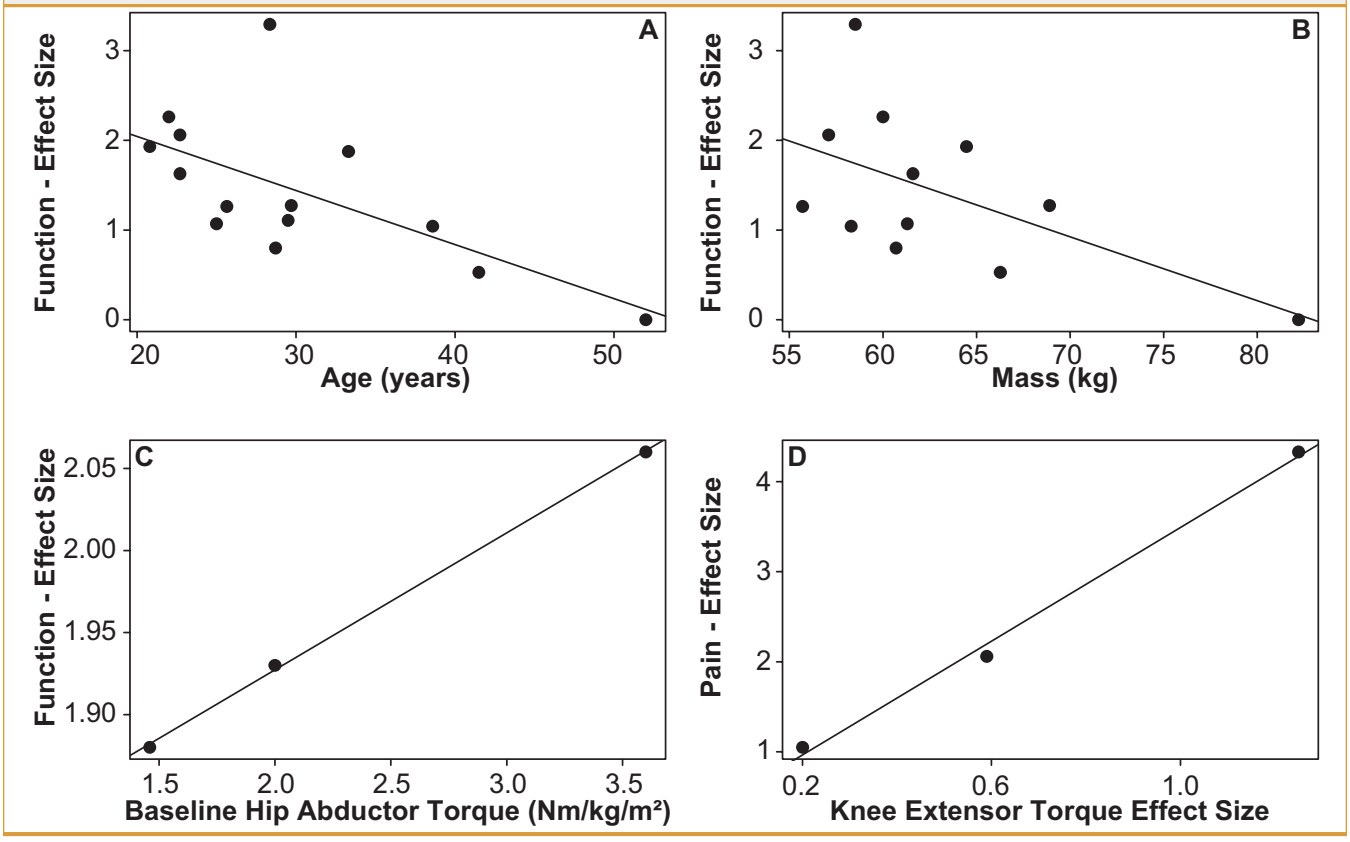
We identified a significant association between effect size for function and lower height (5 RCTs,[5,22,28,39,52] very strong adjusted R^2= 0.98, P = .00; **FIGURE 5B**).

Relationship Between Pain, Function, and Mechanistic Data for Hip-Targeted Exercise Therapy

We identified a significant association between effect size for pain and increased hip abduction strength (4 RCTs,[22,28,39,52] very strong adjusted R^2= 0.93, P = .02) and hip external rotation strength (4 RCTs,[22,28,39,52] very strong adjusted R^2= 0.97, P = .01; **FIGURE 5C-D**).

We identified a significant association between effect size for function and increased hip abduction strength

FIGURE 4
Regression in hip-and-knee–targeted exercise therapy. (A; upper left) Association between effect size for function and older age. (B; upper right) Association between effect size for function and greater mass. (C; bottom left) Association between effect size for function and greater hip abduction torque. (D; bottom right) Association between effect size for pain and increased knee extensor torque.



(4 RCTs,[22,28,39,52] very strong adjusted R^2= 0.96, P = .01) and hip external rotation strength (4 RCTs,[22,28,39,52] very strong adjusted R^2 = 0.96, P = .01; **FIGURE 5E-F**).

We identified a significant association between effect size for function and increased hip abduction strength (4 RCTs,[22,28,39,52] very strong adjusted R^2= 0.96, P = .01) and hip external rotation strength (4 RCTs,[22,28,39,52] very strong adjusted R^2 = 0.96, P = .01; **FIGURE 5E-F**).

DISCUSSION

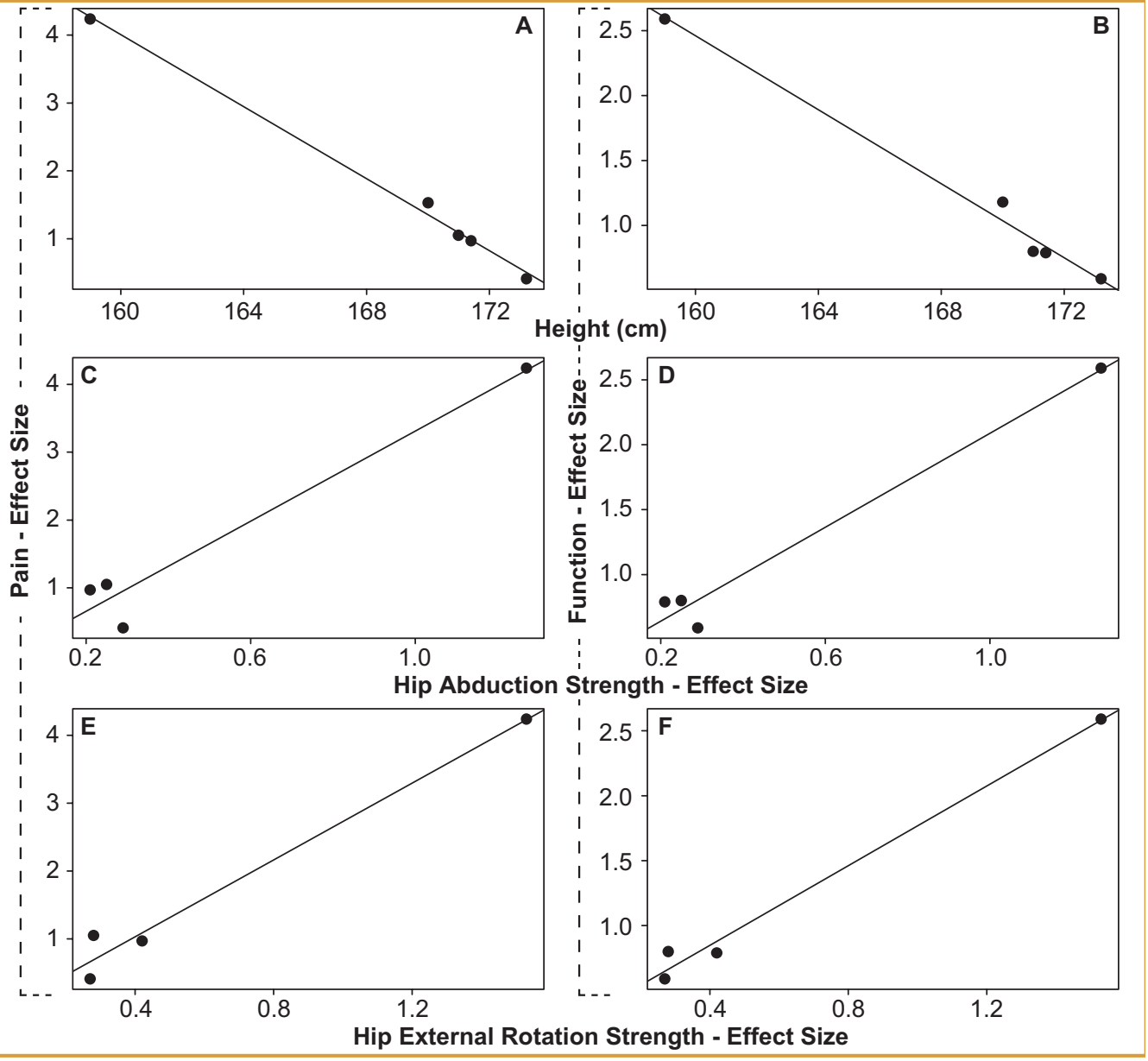
Prolonged symptom duration, older age, greater height and mass, lower baseline knee extensor strength, and higher baseline hip abduction torque were associated with a poorer prognosis in people with PFP. We also identified that increased knee extensor torque and hip abduction and external rotation strength are possible mechanisms of effect in people with PFP. We have identified baseline prognostic and mechanistic variables that should inform future research and may guide physiotherapists in their prescription of exercise therapies in people with PFP. Our results should also guide future research with respect to what mechanistic variables should be prioritized for future research, with regression outcomes becoming more valid as additional data are added.

Prognostic Indicators

Prolonged symptom duration explained 68% of the variance in effect following knee-targeted exercise therapy. This aligns well with previous studies, with Collins et al,[11] reporting that a symptom duration of >2 months is a prognostic indicator for conservative interventions. We also identified that lower age explained 31% of the variance in effect following knee-targeted exercise therapy. This aligns well with the previous systematic review with meta-analysis of Lack et al,[35] who reported that both shorter symptom duration and lower age predict the success of exercise interventions. Clinicians should be aware that younger people with shorter symptom duration have a greater potential to respond favorably to knee-targeted exercise therapy.

Although lower baseline knee extensor strength explained 100% of the variance

FIGURE 5
Regression in hip-targeted exercise therapy. (A; upper left) Association between effect size for pain and lower height. (B; upper right) Association between effect size for function and lower height. (C; middle left) Association between effect size for pain and increased hip abduction strength. (D; middle right) Association between effect size for function and increased hip abduction strength. (E; bottom left) Association between effect size for pain and increased hip external rotation strength. (F; bottom right) Association between effect size for function and increased hip external rotation strength.



in effect following knee-targeted exercise therapy, this is likely explained by the low number of trials included in this regression (n = 3).[22,28,52] There is biological plausibility to this outcome, with epidemiological studies reporting that low quadriceps strength is a risk factor for PFP development,[45] and previous prognostic analyses reporting that people with lower knee strength experience superior functional outcomes in the short term.[35,47] We advise interpreting this outcome as a variable that should be prioritized in future mechanistic work, rather than a variable to guide clinical decision making.

We also identified that lower age explained 68% of the variance in effect following hip-and-knee–targeted exercise therapy, aligning well with our prognos-

tic outcomes for knee-targeted exercise therapy. Lower body mass also explained 28% of the variance in effect following hip-and-knee–targeted exercise therapy, which was not the case for knee-targeted exercise therapy. The overall evidence for the role of body mass in PFP development and persistence is conflicting, with previous epidemiological studies[10,45] reporting that greater body mass is not a predictor of PFP onset, but retrospective analyses typically reporting greater body mass in people with PFP compared to matched controls.[23] This suggests that people with PFP develop greater body mass over time, perhaps due to reduced physical activity as symptoms persist,[20] and clinicians should therefore still consider knee-targeted and hip-and-knee–targeted exercise therapy regardless of their patient's body mass.

Shorter height explained between 98% and 99% of the variance in effect following hip-targeted exercise therapy. It is important to acknowledge that this outcome is the result of regressing data from just,[5,22,28,39,52] but also that the hip-targeted exercise therapy protocols in these trials were very homogeneous. This is a completely novel finding in the PFP field. Shorter people will need to produce lower internal forces to move through maximal joint excursion due to their reduced lever length,[14] possibly allowing them to be adherent without resulting symptom irritability. Muscle cross-sectional area scales to body mass at 0.66 meaning larger (ie, taller) people may be at a detriment by having less muscle mass.[25] Hip-targeted exercise therapy should be considered for people with PFP of all heights, but clinicians may expect greater variability in response as the patient height increases, and the relationship between height and treatment outcome should continue to be explored.

Mechanistic Variables

Increased knee extensor torque explained 99% of the variance in effect following hip-and-knee–targeted exercise therapy, and increasing both hip abduction and hip external rotation strength explained 93% to 97% of the variance in effect following hip-targeted exercise therapy. This must once again be considered in light of the limited number of included trials (n = 3)[1,44,55] and the nuanced understanding that exercise therapy for persistent musculoskeletal conditions is likely to derive its effects though a multifaceted biopsychosocial framework.[6] These outcomes suggest a probable mechanism of effect following exercise protocols in people with PFP, with improved muscle function associated with superior clinical outcomes. This is biologically plausible, particularly increasing knee extensor torque, which would theoretically increase patellofemoral contact area and reduce joint stress.[49] Clinicians should consider if a patient's muscle strength has improved from baseline should they fail to respond positively to exercise therapy.

Nonsignificant Associations

No significant prognostic associations were identified for lower-quadrant manual therapy. This is most explained by the low number of trials from which we could extract prognostic data (n = 3-4), alongside the high variability in outcomes experienced by the participants, with pooled effect sizes ranging from 0.5 to 5.7. We were unable to regress any mechanistic variables extracted from lower quadrant manual therapy trials due to the high heterogeneity in collected measures. No prognostic or mechanistic regressions could be completed for trials of combined interventions for the same reason, and just 2 eligible trials included the use of foot orthoses.

Strengths and Limitations

We only included high-quality trials involving interventions reported to be efficacious to maximize the internal validity of our results. This is the first attempt in the PFP field to use meta-regression to consider both prognostic and mechanistic variables, which is why we chose to regress data from a minimum of 3 high-quality trials instead of requiring a greater volume of data. Care should be taken when interpreting our results with low numbers of included trials, and these outcomes should guide future research more than clinical decision making.

We performed prognostic meta-regressions using typically reported baseline data (eg, symptom duration, body mass, age) but were limited in our ability to perform mechanistic meta-regression from >3 RCTs due to high data heterogeneity. While our study was conducted in adherence to a rigorous methods, there were deviations from our initial PROSPERO-registered protocol, but we are confident that these deviations were necessary and have not influenced the outcome. Future high-quality RCTs should endeavor to report baseline prognostic (eg, hip and knee baseline torque and muscle strength) and intervention mechanistic data (eg, knee extensor torque, hip abduction and external rotation muscle strength) consistent with existing trials in the field to further understanding of why people with PFP may or may not respond to specific interventions.

CONCLUSION

Prolonged symptom duration, older age, taller height and higher mass, lower knee extension strength, and greater baseline hip abduction torque were associated with a poorer prognosis in people with PFP at short-term follow-up after conservative treatment. Increasing knee extensor torque following hip-and-knee–targeted exercise therapy, and hip abduction/external rotation strength following hip-targeted exercise therapy are probable mechanisms of effect in people with PFP. Outcomes involving fewer than

8 trials should be clinically interpreted with caution but guide future research that continues to explore why people with PFP do or do not respond favorably to specific interventions. ■

KEY POINTS

FINDINGS: People with patellofemoral pain who have prolonged symptom durations, higher body mass, and older ages have a poorer prognosis. Increasing hip and knee muscle strength may be a mechanism underpinning exercise therapy.

IMPLICATIONS: This systematic review with meta-regression has identified baseline prognostic and mechanistic variables that may guide physiotherapists in their prescription of exercise therapies in people with patellofemoral pain.

CAUTION: Regressions including low numbers of RCTs should be used to guide future research rather than clinical decision making.

STUDY DETAILS

AUTHOR CONTRIBUTIONS: F.D., A.B.J., N.C., and B.N. were responsible for the conception and design of the study. F.D., S.M.R., and B.N. were responsible for study screening. F.D. and B.N. were responsible for data extraction and analysis. F.D., A.B.J., N.C., and B.N. were responsible for data analysis and interpretation. All the authors finally approved the manuscript. B.N. takes responsibility for the integrity of the work as a whole.

DATA SHARING: All data relevant to the study are included in the article or are available as supplementary files.

PATIENT AND PUBLIC INVOLVEMENT: Not applicable.

REFERENCES

1. Baldon Rde M, Serrao FV, Scattone Silva R, Piva SR. Effects of functional stabilization training on pain, function, and lower extremity biomechanics in women with patellofemoral pain: a randomized clinical trial. *J Orthop Sports Phys Ther.* 2014;44:240-251. https://doi.org/10.2519/jospt.2014.4940
2. Barton CJ, Lack S, Hemmings S, Tufail S, Morrissey D. The 'Best Practice Guide to Conservative Management of Patellofemoral Pain': incorporating level 1 evidence with expert clinical reasoning. *Br J Sports Med.* 2015;49:923-934. https://doi.org/10.1136/bjsports-2014-093637
3. Barton CJ, Lack S, Malliaras P, Morrissey D. Gluteal muscle activity and patellofemoral pain syndrome: a systematic review. *Br J Sports Med.* 2013;47:207-214. https://doi.org/10.1136/bjsports-2012-090953
4. Behrangrad S, Kamali F. Comparison of ischemic compression and lumbopelvic manipulation as trigger point therapy for patellofemoral pain syndrome in young adults: a double-blind randomized clinical trial. *J Bodyw Mov Ther.* 2017;21:554-564. https://doi.org/10.1016/j.jbmt.2016.08.007
5. Bolgla LA, Earl-Boehm J, Emery C, Hamstra-Wright K, Ferber R. Pain, function, and strength outcomes for males and females with patellofemoral pain who participate in either a hip/core-or knee-based rehabilitation program. *Int J Sports Phys Ther.* 2016;11:926-935.
6. Booth J, Moseley GL, Schiltenwolf M, Cashin A, Davies M, Hübscher M. Exercise for chronic musculoskeletal pain: a biopsychosocial approach. *Musculoskelet Care.* 2017;15:413-421. https://doi.org/10.1002/msc.1191
7. Celik D, Argut SK, Türker N, Kilicoglu OI. The effectiveness of superimposed neuromuscular electrical stimulation combined with strengthening exercises on patellofemoral pain: a randomized controlled pilot trial. *J Back Musculoskelet Rehabil.* 2020;33:693-699. https://doi.org/10.3233/BMR-181339
8. Clark D, Downing N, Mitchell J, Coulson L, Syzpryt E, Doherty M. Physiotherapy for anterior knee pain: a randomised controlled trial. *Ann Rheum Dis.* 2000;59:700-704. https://doi.org/10.1136/ard.59.9.700
9. Collins N, Crossley K, Beller E, Darnell R, McPoil T, Vicenzino B. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *BMJ.* 2008;43:169-171. https://doi.org/10.1136/bmj.a1735
10. Collins NJ, Crossley KM, Darnell R, Vicenzino B. Predictors of short and long term outcome in patellofemoral pain syndrome: a prospective longitudinal study. *BMC Musculoskelet Disord.* 2010;11:11. https://doi.org/10.1186/1471-2474-11-11
11. Collins NJ, Bierma-Zeinstra SM, Crossley KM, van Linschoten RL, Vicenzino B, van Middelkoop M. Prognostic factors for patellofemoral pain: a multicentre observational analysis. *Br J Sports Med.* 2013;47:227-233. https://doi.org/10.1136/bjsports-2012-091696
12. Crossley K, Bennell K, Green S, Cowan S, McConnell J. Physical therapy for patellofemoral pain: a randomized, double-blinded, placebo-controlled trial. *Am J Sports Med.* 2002;30:857-865. https://doi.org/10.1177/03635465020300061701
13. Das RK, Malik KKU, Sarkar B, Saha S, Biswas A. Efficacy of neuromuscular electrical stimulation on vastus medialis obliqus in patellofemoral pain syndrome: a double blinded randomized controlled trail. *Int J Ther Rehabil.* 2016;5:149-156. https://doi.org/10.5455/ijtrr.000000198
14. Dvir Z, Müller S. Multiple-joint isokinetic dynamometry: a critical review. *J Strength Cond Res.* 2020;34:587-601. https://doi.org/10.1519/jsc.0000000000002982
15. Eijkenboom JFA, Waarsing JH, Oei EHG, Bierma-Zeinstra SMA, van Middelkoop M. Is patellofemoral pain a precursor to osteoarthritis?: patellofemoral osteoarthritis and patellofemoral pain patients share aberrant patellar shape compared with healthy controls. *Bone Joint Res.* 2018;7:541-547. https://doi.org/10.1302/2046-3758.79.Bjr-2018-0112.R1
16. Espí-López GV, Serra-Añó P, Vicent-Ferrando J, et al. Effectiveness of inclusion of dry needling in a multimodal therapy program for patellofemoral pain: a randomized parallel-group trial. *J Orthop Sports Phys Ther.* 2017;47:392-401. https://doi.org/10.2519/jospt.2017.7389
17. Fukuda TY, Melo WP, Zaffalon BM, et al. Hip posterolateral musculature strengthening in sedentary women with patellofemoral pain syndrome: a randomized controlled clinical trial with 1-year follow-up. *J Orthop Sports Phys Ther.* 2012;42:823-830. https://doi.org/10.2519/jospt.2012.4184
18. Fukuda TY, Rossetto FM, Magalhaes E, Bryk FF, Lucareli PR, de Almeida Aparecida Carvalho N. Short-term effects of hip abductors and lateral rotators strengthening in females with patellofemoral pain syndrome: a randomized controlled clinical trial. *J Orthop Sports Phys Ther.* 2010;40:736-742. https://doi.org/10.2519/jospt.2010.3246
19. García-Triana SA, Toro-Sashida MF, Larios-González XV, et al. The benefit of perineural injection treatment with dextrose for treatment of chondromalacia patella in participants receiving home physical therapy: a pilot randomized clinical trial. *J Altern Complement Med.* 2021;27:38-44. https://doi.org/10.1089/acm.2020.0287
20. Glaviano NR, Baellow A, Saliba S. Physical activity levels in individuals with and without patellofemoral pain. *Phys Ther Sport.* 2017;27:12-16. https://doi.org/10.1016/j.ptsp.2017.07.002
21. Halabchi F, Mazaheri R, Mansournia MA, Hamedi Z. Additional effects of an individualized risk factor–based approach on pain and the function of patients with patellofemoral pain syndrome: a randomized controlled trial. *Clin J Sport Med.* 2015;25:478-486. https://doi.org/10.1097/JSM.0000000000000177
22. Hansen R, Brushøj C, Rathleff MS, Magnusson SP, Henriksen M. Quadriceps or hip exercises for patellofemoral pain? A randomised controlled equivalence trial. *Br J Sports Med.* 2023;57:1287-1294. https://doi.org/10.1136/bjsports-2022-106197

23. Hart HF, Barton CJ, Khan KM, Riel H, Crossley KM. Is body mass index associated with patellofemoral pain and patellofemoral osteoarthritis? A systematic review and meta-regression and analysis. *Br J Sports Med.* 2017;51:781-790. https://doi.org/10.1136/bjsports-2016-096768
24. Hasan S, Alonazi A, Anwer S, et al. Efficacy of patellar taping and electromyographic biofeedback training at various knee angles on quadriceps strength and functional performance in young adult male athletes with patellofemoral pain syndrome: a randomized controlled trial. *Pain Res Manag.* 2022;2022:8717932. https://doi.org/10.1155/2022/8717932
25. Heymsfield SB, Hwaung P, Ferreyro-Bravo F, Heo M, Thomas DM, Schuna JM Jr. Scaling of adult human bone and skeletal muscle mass to height in the US population. *Am J Hum Biol.* 2019;31:e23252. https://doi.org/10.1002/ajhb.23252
26. Higgins JP, Green S. *Cochrane handbook for systematic reviews of interventions*. Wiley, 2008. https://doi.org/10.1002/9780470712184
27. Hossein HS, Sara A, Hasan D, Navid K. The effect of three types of exercises programs on the patella location in athletes with patellofemoral pain. *Knee.* 2023;41:97-105. https://doi.org/10.1016/j.knee.2022.12.014
28. Hott A, Brox JI, Pripp AH, Juel NG, Paulsen G, Liavaag S. Effectiveness of isolated hip exercise, knee exercise, or free physical activity for patellofemoral pain: a randomized controlled trial. *Am J Sports Med.* 2019;47:1312-1322. https://doi.org/10.1177/0363546519830644
29. Hott A, Brox JI, Pripp AH, Juel NG, Liavaag S. Patellofemoral pain: one year results of a randomized trial comparing hip exercise, knee exercise, or free activity. *Scand J Med Sci Sports.* 2020;30:741-753. https://doi.org/10.1111/sms.13613
30. Ismail MM, Gamaleldein MH, Hassa KA. Closed kinetic chain exercises with or without additional hip strengthening exercises in management of patellofemoral pain syndrome: a randomized controlled trial. *Eur J Phys Rehabil Med.* 2013;49:687-698.
31. Jenkins DG, Quintana-Ascencio PF. A solution to minimum sample size for regressions. *PLOS ONE.* 2020;15:e0229345. https://doi.org/10.1371/journal.pone.0229345
32. Karamiani F, Mostamand J, Rahimi A, Nasirian M. The effect of gluteus medius dry needling on pain and physical function of non-athlete women with unilateral patellofemoral pain syndrome: a double-blind randomized clinical trial. *J Bodyw Mov Ther.* 2022;30:23-29. https://doi.org/10.1016/j.jbmt.2022.02.005
33. Kisacik P, Tunay VB, Bek N, Karaduman AA. Is there any additional effect of foot core training on dynamic function and balance in women with patellofemoral pain? A randomized controlled study. *Sport Sci Health.* 2024;20:137-143. https://doi.org/10.1007/s11332-023-01076-6
34. Kumar V, Subramanian NB, Sreelatha S, Kotamraju S, Krishnan M. Physiotherapeutic interventions on quadriceps muscle architecture in patello-femoral pain syndrome. *Bioinformation.* 2023;19:454-459. https://doi.org/10.6026/97320630019454
35. Lack S, Barton C, Vicenzino B, Morrissey D. Outcome predictors for conservative patellofemoral pain management: a systematic review and meta-analysis. *Sports Med.* 2014;44:1703-1716. https://doi.org/10.1007/s40279-014-0231-5
36. Lankhorst N, van Middelkoop M, Crossley K, et al. Factors that predict a poor outcome 5–8 years after the diagnosis of patellofemoral pain: a multicentre observational analysis. *Br J Sports Med.* 2015;50:881-886. https://doi.org/10.1136/bjsports-2015-094664
37. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther.* 2003;83:713-721. https://doi.org/10.1093/ptj/83.8.713
38. Matthews M, Rathleff MS, Claus A, et al. Can we predict the outcome for people with patellofemoral pain? A systematic review on prognostic factors and treatment effect modifiers. *Br J Sports Med.* 2016;51:1650-1660. https://doi.org/10.1136/bjsports-2016-096545
39. Matthews M, Rathleff MS, Claus A, et al. Does foot mobility affect the outcome in the management of patellofemoral pain with foot orthoses versus hip exercises? A randomised clinical trial. *Br J Sports Med.* 2020;54:1416-1422. https://doi.org/10.1136/bjsports-2019-100935
40. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med.* 2009;151:264-W64. https://doi.org/10.7326/0003-4819-151-4-200908180-00135
41. Mølgaard CM, Rathleff MS, Andreasen J, et al. Foot exercises and foot orthoses are more effective than knee focused exercises in individuals with patellofemoral pain. *J Sci Med Sport.* 2018;21:10-15. https://doi.org/10.1016/j.jsams.2017.05.019
42. Moseley AM, Herbert RD, Maher CG, Sherrington C, Elkins MR. Reported quality of randomized controlled trials of physiotherapy interventions has improved over time. *J Clin Epidemiol.* 2011;64:594-601. https://doi.org/10.1016/j.jclinepi.2010.08.009
43. Motealleh A, Mohamadi M, Moghadam MB, Nejati N, Arjang N, Ebrahimi N. Effects of core neuromuscular training on pain, balance, and functional performance in women with patellofemoral pain syndrome: a clinical trial. *J Chiropr Med.* 2019;18:9-18. https://doi.org/10.1016/j.jcm.2018.07.006
44. Nakagawa TH, Muniz TB, Baldon Rde M, Dias Maciel C, de Menezes Reiff RB, Serrao FV. The effect of additional strengthening of hip abductor and lateral rotator muscles in patellofemoral pain syndrome: a randomized controlled pilot study. *Clin Rehabil.* 2008;22:1051-1060. https://doi.org/10.1177/0269215508095357
45. Neal BS, Lack SD, Lankhorst NE, Raye A, Morrissey D, van Middelkoop M. Risk factors for patellofemoral pain: a systematic review and meta-analysis. *Br J Sports Med.* 2019;53:270-281. https://doi.org/10.1136/bjsports-2017-098890
46. Neal BS, Bartholomew C, Barton CJ, Morrissey D, Lack SD. Six treatments have positive effects at 3 months for people with patellofemoral pain: a systematic review with meta-analysis. *J Orthop Sports Phys Ther.* 2022;52:750-768. https://doi.org/10.2519/jospt.2022.11359
47. Pattyn E, Mahieu N, Selfe J, Verdonk P, Steyaert A, Witvrouw E. What predicts functional outcome after treatment for patellofemoral pain? *Med Sci Sports Exerc.* 2012;44:1827-1833. https://doi.org/10.1249/MSS.0b013e31825d56e3
48. Pompeo KD, da Rocha ES, Melo MA, et al. Can we replace exercises targeted on core/hip muscles by exercises targeted on leg/foot muscles in women with patellofemoral pain? A randomized controlled trial. *Phys Ther Sport.* 2022;58:1-7. https://doi.org/10.1016/j.ptsp.2022.08.004
49. Powers CM, Witvrouw E, Davis IS, Crossley KM. Evidence-based framework for a pathomechanical model of patellofemoral pain: 2017 patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester, UK: part 3. *Br J Sports Med.* 2017;51:1713-1723. https://doi.org/10.1136/bjsports-2017-098717
50. Rasti E, Rojhani-Shirazi Z, Ebrahimi N, Sobhan MR. Effects of whole body vibration with exercise therapy versus exercise therapy alone on flexibility, vertical jump height, agility and pain in athletes with patellofemoral pain: a randomized clinical trial. *BMC Musculoskelet Disord.* 2020;21:1-9. https://doi.org/10.1186/s12891-020-03732-1
51. Rosnow RL, Rosenthal R, Rubin DB. Contrasts and correlations in effect-size estimation. *Psychol Sci.* 2000;11:446-453. https://doi.org/10.1111/1467-9280.00287
52. Saad MC, de Vasconcelos RA, de Oliveira Mancinelli LV, de Barros Munno MS, Liporaci RF, Grossi DB. Is hip strengthening the best treatment option for females with patellofemoral pain? A randomized controlled trial of three different types of exercises. *Braz J Phys Ther.* 2018;22:408-416. https://doi.org/10.1016/j.bjpt.2018.03.009
53. Şahin M, Ayhan FF, Borman P, Atasoy H. The effect of hip and knee exercises on pain, function, and strength in patientswith patellofemoral pain syndrome: a randomized controlled trial. *Turk J Med Sci.* 2016;46:265-277. https://doi.org/10.3906/sag-1409-66
54. Schober P, Boer C, Schwarte LA. Correlation coefficients: appropriate use and interpretation. *Anesth Analg.* 2018;126:1763-1768. https://doi.org/10.1213/ANE.0000000000002864
55. Silva NC, de Castro Silva M, Tamburús NY, Guimarães MG, de Oliveira Nascimento MB, Felicio LR. Adding neuromuscular training to a strengthening program did not produce additional improvement in clinical or kinematic outcomes in women with patellofemoral pain: a blinded randomised controlled trial. *Musculoskelet Sci Pract.* 2023;63:102720. https://doi.org/10.1016/j.msksp.2023.102720
56. Smith BE, Selfe J, Thacker D, et al. Incidence and prevalence of patellofemoral pain: a

systematic review and meta-analysis. *PLOS ONE.* 2018;13:e0190892. https://doi.org/https://doi.org/10.1371/journal.pone.0190892

57. Song CY, Lin YF, Wei TC, Lin DH, Yen TY, Jan MH. Surplus value of hip adduction in leg-press exercise in patients with patellofemoral pain syndrome: a randomized controlled trial. *Phys Ther.* 2009;89:409-418. https://doi.org/10.2522/ptj.20080195

58. Tazesh B, Mansournia MA, Halabchi F. Additional effects of core stability exercises on pain and function of patients with patellofemoral pain: a randomized controlled trial. *J orthop Trauma Rehabil.* 2022;29. https://doi.org/10.1177/2210491721989075

59. Van den Dolder PA, Roberts DL. Six sessions of manual therapy increase knee flexion and improve activity in people with anterior knee pain: a randomised controlled trial. *Aust J Physiother.* 2006;52:261-264. https://doi.org/10.1016/s0004-9514(06)70005-8

60. Willy RW, Hoglund LT, Barton CJ, et al. Patellofemoral pain. *J Orthop Sports Phys Ther.* 2019;49:CPG1-CPG95. https://doi.org/10.2519/jospt.2019.0302

61. Wu Z, Zou Z, Zhong J, et al. Effects of whole-body vibration plus hip-knee muscle strengthening training on adult patellofemoral pain syndrome: a randomized controlled trial. *Disabil Rehabil.* 2022;44:6017-6025. https://doi.org/10.1080/09638288.2021.1954703

62. Yañez-Álvarez A, Bermúdez-Pulgarín B, Hernández-Sánchez S, Albornoz-Cabello M. Effects of exercise combined with whole body vibration in patients with patellofemoral pain syndrome: a randomised-controlled clinical trial. *BMC Musculoskelet Disord.* 2020;21:1-11. https://doi.org/10.1186/s12891-020-03599-2

63. Zafarian T, Taghipour M, Khafri S, Bahrami M, Javanshir K. The effect of lumbopelvic manipulation on electromyography parameters of gluteus medius and vastus medialis in patients with patellofemoral pain syndrome: a double-blind, placebo-controlled trial. *Int J Osteopath Med.* 2023;50:100667. https://doi.org/10.1016/j.ijosm.2023.100667

64. Zago J, Amatuzzi F, Rondinel T, Matheus JP. Osteopathic manipulative treatment versus exercise program in runners with patellofemoral pain syndrome: a randomized controlled trial. *J Sport Rehabil.* 2020;30:609-618. https://doi.org/10.1123/jsr.2020-0108

65. Zarei H, Bervis S, Piroozi S, Motealleh A. Added value of gluteus medius and quadratus lumborum dry needling in improving knee pain and function in female athletes with patellofemoral pain syndrome: a randomized clinical trial. *Arch Phys Med Rehabil.* 2020;101:265-274. https://doi.org/10.1016/j.apmr.2019.07.009