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Progressive Resistance Training or Neuromuscular Exercise for Hip Osteoarthritis

A Multicenter Cluster Randomized Controlled Trial

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Background: Exercise is recommended as first-line treatment for patients with hip osteoarthritis (OA). However, randomized controlled trials providing evidence for the optimal exercise type are lacking.

Objective: To investigate whether progressive resistance training (PRT) is superior to neuromuscular exercise (NEMEX) for improving functional performance in patients with hip OA.

Design: Multicenter, cluster-randomized, controlled, parallel-group, assessor-blinded, superiority trial. (ClinicalTrials.gov: NCT04714047)

Setting: Hospitals and physiotherapy clinics.

Participants: 160 participants with clinically diagnosed hip OA were enrolled from 18 January 2021 to 28 April 2023 and randomly assigned to PRT ($n = 82$) or NEMEX ($n = 78$).

Intervention: Twelve weeks of PRT or NEMEX with 2 supervised 60-minute group sessions each week. The PRT intervention consisted of 5 high-intensity resistance training exercises targeting muscles at the hip and knee joints. The NEMEX intervention included 10 exercises and emphasized sensorimotor control and functional stability.

Measurements: The primary outcome was change in the 30-second chair stand test (30s-CST). Key secondary outcomes were changes in scores on the pain and hip-related quality of life (QoL) subscales of the Hip Disability and Osteoarthritis Outcome Score (HOOS).

Results: The mean changes from baseline to 12-week follow-up in the 30s-CST were 1.5 (95% CI, 0.9 to 2.1) chair stands with PRT and 1.5 (CI, 0.9 to 2.1) chair stands with NEMEX (difference, 0.0 [CI, −0.8 to 0.8] chair stands). For the HOOS pain subscale, mean changes were 8.6 (CI, 5.3 to 11.8) points with PRT and 9.3 (CI, 5.9 to 12.6) points with NEMEX (difference, −0.7 [CI, −5.3 to 4.0] points). For the HOOS QoL subscale, mean changes were 8.0 (CI, 4.3 to 11.7) points with PRT and 5.7 (CI, 1.9 to 9.5) points with NEMEX (difference, 2.3 [CI, −3.0 to 7.6] points).

Limitation: Participants and physiotherapists were not blinded.

Conclusion: In patients with hip OA, PRT is not superior to NEMEX for improving functional performance, hip pain, or hip-related QoL.

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Hip osteoarthritis (OA) is a degenerative joint disease that results in hip pain and impaired muscle strength, physical function, range of motion, and quality of life (QoL) (1). Its prevalence has been reported to be nearly 10% in people aged 45 years or older (2) and is expected to increase due to demographic changes (3). This represents a substantial and increasing global burden on health care systems, and identifying the most effective treatments for hip OA is essential (3).

High-quality evidence has shown that exercise is effective in reducing pain and improving physical function in hip OA (4, 5), and clinical guidelines recommend exercise as first-line treatment (6). However, randomized controlled trials providing evidence for the optimal exercise content and dosage are lacking (4, 5). Consequently, it is currently not possible to recommend one type of exercise over another (7, 8).

Neuromuscular exercise (NEMEX), an exercise program that targets functional stability and postural control, can reduce pain and improve physical function and QoL in patients with hip OA (9, 10). It has been implemented in several countries as part of the Good Life with osteoArthritis in Denmark (GLA:D) initiative (11). However, NEMEX has not been compared with other types of exercise in hip OA. Progressive resistance training (PRT) is another promising exercise type that is effective at reducing pain and improving physical function and QoL in hip OA (12, 13). Of note, PRT is considered the most potent intervention for increasing muscle mass, strength, and power (14, 15), features that are markedly hampered in hip OA and closely related to

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physical function (16–18). This suggests that PRT may be more effective than NEMEX in improving physical function; therefore, a head-to-head comparison is justified.

The primary objective of this randomized controlled trial was to investigate the effectiveness of 12 weeks of PRT compared with NEMEX on functional performance in patients with hip OA. The primary hypothesis was that PRT is superior to NEMEX at improving functional performance, measured by the 30-second chair stand test (30s-CST). Key secondary outcomes were patient-reported pain and hip-related QoL.

METHODS

Trial Design

This multicenter, cluster-randomized, controlled, parallel-group, assessor-blinded, superiority trial was conducted at 5 hospitals and 10 physiotherapy clinics across 3 of 5 health care regions in Denmark. Participants were enrolled from 18 January 2021 to 28 April 2023. After baseline assessment, participants were randomly assigned in groups of 3 to 5 people to 12 weeks of PRT or NEMEX, with or without booster sessions provided at 4, 6, 8, and 10 months after baseline. This article reports outcomes measured at baseline and at 12-week follow-up from the PRT and NEMEX groups. Further details of the trial design have been published in the trial protocol (19). Reporting is in accordance with the CONSORT (Consolidated Standards of Reporting Trials) guidelines (20). Outcomes with booster sessions will be reported in a separate article.

Participants

Patients were screened for eligibility and provided with information about the trial at physiotherapy clinics or orthopedic departments at the participating hospitals. Those who met the inclusion criteria and agreed to participate were asked to provide written informed consent, completed the baseline assessments, and were then randomly assigned to 12 weeks of PRT or NEMEX with or without booster sessions. This article reports the findings from the initial 12-week follow-up after PRT or NEMEX.

Inclusion criteria were 1) clinically diagnosed OA of 1 or both hip joints according to the National Institute for Health and Care Excellence criteria (21), 2) an event of pain during activity that was rated at least 3 on a 10-point numerical rating scale in the index hip within the previous 2 weeks, 3) age 45 years or older, 4) no or less than 30 minutes of hip joint stiffness in the morning, 5) no surgery in the lower extremities 6 months before inclusion, 6) no comorbidity that markedly affected hip function, 7) adequate fluency in written and spoken Danish, and 8) not being a candidate for total hip arthroplasty. Exclusion criteria were 1) body mass index above 40 kg/m^2, 2) pregnancy, 3) PRT or NEMEX for the lower extremities exceeding 12 sessions over the previous 6 months or 6 sessions over the previous 3 months, and 4) planned vacation for more than 14 days within the initial 12-week intervention period with no possibility of extending the intervention accordingly.

Randomization

After baseline assessment, participants were randomly assigned to either PRT or NEMEX, with or without booster sessions, via cluster randomization stratified by recruitment site according to a randomly generated sequence of numbers. We combined all participants receiving PRT with or without booster sessions and those receiving NEMEX with or without booster sessions into 2 groups (PRT and NEMEX). A member of the research team (I.M.) who was not involved in recruitment, assessment, or treatment generated the allocation sequence for each of the sites by drawing tokens from a bag containing an even distribution of the allocations. The sequence was concealed from the physiotherapists, nurses, and surgeons who screened and recruited participants. When a sufficient number of participants had been enrolled and assessed at baseline to form a cluster, the principal investigator (T.K.) informed the site manager at the specific site about the allocation for that cluster. The cluster size was set at 5 participants, and all participants in each group attended all exercise sessions together. To ensure an acceptable waiting time, groups of 1 to 4 participants were cluster-randomized if they had waited more than 2 weeks after inclusion.

Blinding

Outcome assessors were blinded to treatment allocation. Participants were instructed not to reveal their allocation at 12-week assessments. Participants and physiotherapists supervising the interventions could not be blinded to treatment allocation. The statistical analyses and interpretation of primary and key secondary outcomes were blinded to treatment allocation (22), and a signed interpretation document was uploaded before unblinding (23).

Interventions

The exercise interventions were provided at the hospitals and physiotherapy clinics by physiotherapists trained in delivering the program as described in the trial protocol (19) and in **Appendix Table 1** and **Appendix Figure 1** (available at Annals.org). All sessions were conducted as group sessions with 1 physiotherapist supervising the exercises. The duration and frequency of the interventions was 12 weeks with 2 supervised 60-minute sessions each week separated by at least 72 hours. Each session consisted of a 10-minute submaximal warm-up on an exercise bike at an intensity of 13 to 14 on the Borg Rating of Perceived Exertion scale (24), followed by 50 minutes of PRT or NEMEX. If participants experienced pain during an exercise with an intensity exceeding 5 out of 10 on a numerical rating scale, the physiotherapist modified that exercise (**Appendix Table 1**). All unilateral exercises were performed with both legs. No restrictions were applied for concomitant care.

Neuromuscular Exercise

The NEMEX intervention was performed in accordance with the program described by Ageberg and colleagues, emphasizing sensorimotor control and functional stability (19, 25). Briefly, 10 exercises were performed each session, and progression was based on 4 levels of difficulty by varying the number, direction, and velocity of the movements and/or changing the support surface (25, 26).

Progressive Resistance Training

The PRT intervention consisted of 5 generic exercises performed each session that targeted the muscles of the hip and knee joints, with emphasis on maximizing intensity (load) of the exercises following the repetition maximum principle (load increased when the target number of repetitions can be completed) and training to muscle failure (19, 27). The progression followed linear periodization in line with the guidelines of the American College of Sports Medicine (14, 28). For the third set of every exercise, participants were instructed to continue until volitional muscle failure, and whenever the intended number of repetitions in the third set were completed, the exercise intensity (load) was increased by 2% to 10%.

Outcomes

Outcome measures were assessed at the participating hospitals at baseline and within 1 week after the interventions by physiotherapists trained according to a standardized protocol.

Primary Outcome

The primary outcome was change in the 30s-CST from baseline to 12-week follow-up. The 30s-CST is a valid, responsive, and reliable test for evaluating sit-to-stand function (number of repetitions) (29–32). Identical chairs (seat height of 44 cm with no armrests) were provided for each test location. A major clinically important difference (MaCID) for the 30s-CST of 2.1 chair stands was defined by Wright and colleagues (33).

Key Secondary Outcomes

Key secondary outcomes were changes in the pain and hip-related QoL subscales of the Hip Disability and Osteoarthritis Outcome Score (HOOS) from baseline to 12-week follow-up. The HOOS is a 40-item patient-reported questionnaire consisting of 5 subscales, each scored from 0 (worst) to 100 (best) (34). The HOOS is a valid, reliable, and responsive measure in patients with hip OA (35). The pain and hip-related QoL subscales were chosen a priori as key secondary outcomes (19).

Other Secondary Outcomes

Other secondary outcomes were changes from baseline to 12-week follow-up in the HOOS subscales for symptoms, activities of daily living (ADL), and function in sports and recreational activities (34); the 40-meter fast-paced walk test (33); the 9-step timed stair climb test (36); unilateral leg extensor muscle power, measured with the Nottingham leg extensor power rig (36, 37); unilateral 1-repetition maximum (1RM) leg press strength for the more affected limb (38); global perceived effect (GPE) for pain, ADL, and QoL (39); and differences in adverse events and serious adverse events, adherence to interventions, and dropouts.

Sample Size

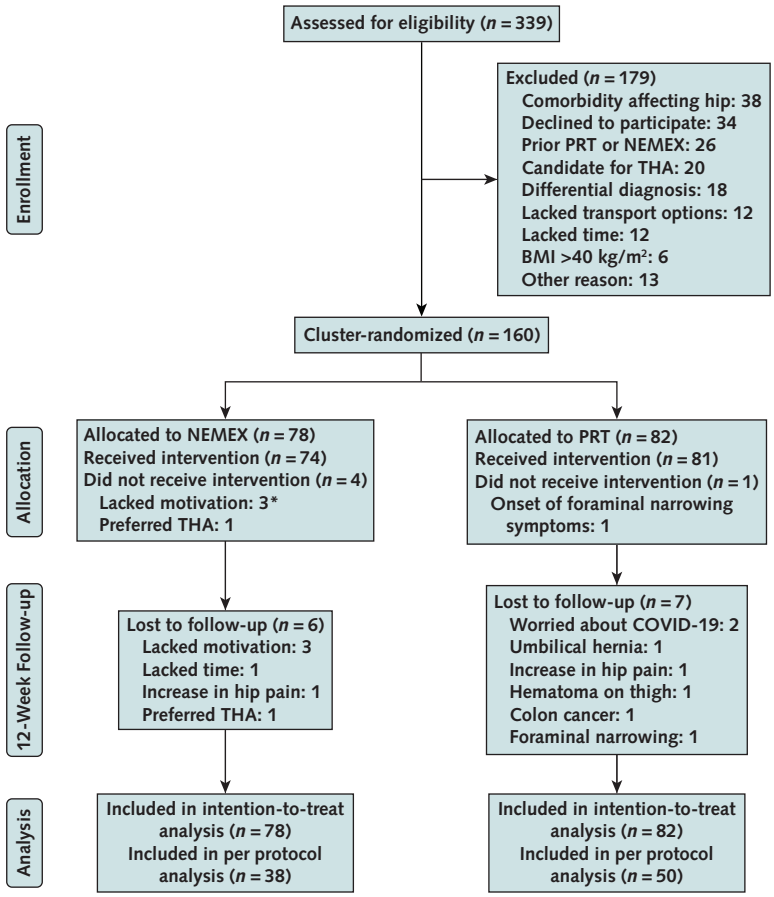
The sample size calculation was based on the expected between-group difference in the 30s-CST from baseline to 12-week follow-up. Due to a lack of data specifically on hip OA, the sample size calculation relied on knee OA data (40, 41). To detect a difference of 1.5 chair stands and a standard deviation of 2.52 given a power of 0.90, a 2-sided significance level of 0.05, and an anticipated dropout rate of 30%, the total sample size was estimated to be 160 participants. Because the MaCID for the between-group difference is larger than the mean difference that this trial is powered to detect, the statistical power is greater than what is required to detect a mean difference of 2.1.

Statistical Analysis

Statistical analyses were performed as described a priori in the statistical analysis plan that was uploaded to ClinicalTrials.gov (NCT04714047). An intention-to-treat approach that included all randomly assigned participants was used to analyze all changes in primary and secondary outcome measures. Between-group comparisons of change from baseline to follow-up in the primary and secondary continuous outcomes were analyzed using a repeated-measures mixed model with participants, clusters, and sites as random effects and visits and treatment group as fixed effects. A per protocol analysis was conducted for participants who had high adherence to the interventions (≥80%), had high exercise fidelity (≥80% of prescribed sets performed), and had not undergone hip surgery. In addition, inverse probability–weighted regression adjustment analyses were performed to address potential influences of bias in per protocol analyses. The statistical level of significance was set to a P value less than 0.05. All analyses were performed in Stata, version 17 (StataCorp).

To further guide the clinical interpretation of change in 30s-CST, the between-group difference in the proportion of participants achieving the major clinically important improvement (MaCII) of 2.6 chair stands for within-patient score change, as defined by Wright and colleagues (33), was analyzed using a threshold of 20% (42). A difference of less than 20% was considered no meaningful difference between treatments, and 20% or greater was considered a meaningful difference (42). Furthermore, we calculated the trial-specific minimal important difference (MID) by subtracting the mean score for participants who reported having experienced a "small but not important change" in GPE

Figure. Flowchart of enrollment, randomization, treatment, and follow-up of trial participants.



Eleven participants discontinued the intervention and may or may not have been lost to follow-up (4 in the NEMEX group [2 who lacked time, 1 who lacked motivation, and 1 who had an increase in hip pain] and 7 in the PRT group [2 who were worried about COVID-19, 1 who lacked time, 1 who had back pain, 1 who had an increase in hip pain, 1 who had a hematoma on the thigh, and 1 who had colon cancer]). BMI = body mass index; NEMEX = neuromuscular exercise; PRT = progressive resistance training; THA = total hip arthroplasty.
* One participant did not receive any intervention but agreed to participate in the 12-week follow-up as per the intention-to-treat approach.

from the mean score for those reporting an "important change" in GPE (Supplement Table 1, available at Annals.org). In the absence of existing clinically relevant thresholds for the key secondary outcomes, trial-specific minimal important changes (MICs) were estimated post hoc using the predictive modeling approach (43).

Ethics

The trial protocol was approved by the Central Denmark Region Committee on Health Research Ethics (Journal No. 1-10-72-267-20) and registered at ClinicalTrials.gov (NCT04714047) and the Danish Data Protection Agency (Journal No. 1-16-02-11-21) before inclusion of participants.

Role of the Funding Source

The trial was funded by the Independent Research Fund Denmark, Fysioterapipraksisfonden, Helsefonden, Aarhus University, Region Zealand, The Association of Danish Physiotherapists, Andelsfonden, and Familien Hede Nielsens Fond. The funders had no influence on the design, conduct, or interpretation of the trial.

RESULTS

Participants

From a total of 339 patients who were screened for eligibility from January 2021 to April 2023 (Figure), 160 were included and randomly assigned to PRT (n = 82) or NEMEX (n = 78). There were 37 clusters with 3 or more participants and 5 clusters with 2 or fewer participants. The only meaningful difference between the PRT and NEMEX groups at baseline was in the proportion of participants recruited from a hospital (Table 1). Consequently, sensitivity analyses were conducted by including recruitment site as a fixed effect in the mixed-effects model for the primary and key secondary outcomes. There were no changes in between-group differences when the results were rounded to 1 decimal point (Appendix Table 2, available at Annals.org).

Table 1. Characteristics of Included Patients at the Time of Baseline Testing

Characteristic	NEMEX ($n = 78$)	PRT ($n = 82$)
Female, *n (%)*	48 (62)	56 (68)
Mean age (SD), *y*	63.9 (9.1)	66.1 (7.4)
Mean BMI (SD), *kg/m²*	27.7 (4.6)	28.2 (4.6)
Hip osteoarthritis, *n (%)*		
Unilateral	54 (69)	62 (76)
Bilateral	24 (31)	20 (24)
Duration of symptoms, *n (%)*		
0–1 y	15 (19)	17 (21)
>1–2 y	20 (26)	21 (26)
>2–5 y	33 (42)	26 (32)
>5 y	10 (13)	18 (22)
Civil status, *n (%)*		
Married or cohabiting	58 (74)	63 (77)
Single	20 (26)	19 (23)
Education level, *n (%)*		
Primary school	6 (8)	10 (12)
High school or similar	4 (5)	2 (2)
Vocational education	30 (38)	27 (33)
Higher education	38 (49)	43 (52)
Employment status, *n (%)*		
Employed or self-employed	29 (37)	33 (40)
Unemployed	8 (10)	8 (10)
Retired	41 (53)	41 (50)
Smoking status, *n (%)*		
Never	33 (42)	35 (41)
Former	37 (47)	40 (49)
Current	8 (10)	7 (9)
Previous treatment, *n (%)*		
Exercise	9 (12)	13 (16)
Physiotherapy	17 (22)	25 (30)
Chiropractic	5 (6)	9 (11)
Corticosteroid injection	5 (6)	6 (7)
Previous surgery, *n (%)*		
Contralateral THA	3 (4)	2 (2)
Hip arthroscopy	3 (4)	0 (0)
Internal fixation of fracture	1 (1)	1 (1)
Use of analgesics, *n (%)*		
Acetaminophen	41 (53)	52 (63)
Nonsteroidal anti-inflammatory drugs	25 (32)	23 (28)
Morphine or opioids	2 (3)	1 (1)
Other	5 (6)	7 (9)
Comorbidities, *n (%)*		
Knee osteoarthritis	2 (3)	2 (2)
Type 2 diabetes	4 (5)	3 (4)
Hypertension	5 (6)	5 (6)
Osteoporosis	2 (3)	2 (2)
Asthma	3 (4)	8 (10)
Other less frequent comorbidity*	18 (NA)	19 (NA)
Physical activity (weekly), *n (%)*		
≥150 min, moderate intensity	32 (41)	33 (40)
≥60 min, vigorous intensity	25 (32)	18 (22)
≥90 min, vigorous intensity	13 (17)	12 (15)
Sedentary behavior (daily), *n (%)*		
≥10 h	15 (19)	19 (23)
≥7 h	30 (38)	36 (44)
Recruitment site, *n (%)*		
Hospital	32 (41)	16 (20)
Physiotherapy clinic	46 (59)	66 (80)
Treatment site, *n (%)*		
Hospital	19 (24)	8 (10)
Physiotherapy clinic	59 (76)	74 (90)

BMI = body mass index; NA = not applicable; NEMEX = neuromuscular exercise; PRT = progressive resistance training; THA = total hip arthroplasty.
* Includes chronic obstructive pulmonary disease, migraine, and osteoarthritis of joints other than the hip and knee (each with a total $n < 4$).

During the study, 13 (8%) participants dropped out (7 from the PRT group [9%] and 6 from the NEMEX group [8%]). When invited to the first exercise session, 5 participants declined initiating the intervention (1 who had onset of foraminal narrowing symptoms in the PRT group, and 3 who lacked motivation to exercise and 1 who preferred total hip arthroplasty in the NEMEX group). During the interventions, 11 (7%) participants declined to continue exercising (7 in the PRT group and 4 in the NEMEX group).

Primary Outcome: 30s-CST

The mean change in the 30s-CST from baseline to 12-week follow-up was 1.5 (95% CI, 0.9 to 2.1) chair stands in the PRT group and 1.5 (CI, 0.9 to 2.1) chair stands in the NEMEX group (Table 2; Appendix Figure 2, available at Annals.org). The mean between-group difference was 0.0 (CI, −0.8 to 0.8) chair stands, which was below the MaCID of 2.1 chair stands (33) and the trial-specific MID of 0.5 chair stands. The proportion of participants attaining the MaCII of 2.6 chair stands was 41.5% in the PRT group and 37.2% in the NEMEX group, with a between-group difference of 4.3 (CI, −11.0 to 19.4) percentage points, which was less than the a priori–defined meaningful difference of 20 percentage points (19).

Key Secondary Outcomes: HOOS Pain and Hip-Related QoL Subscales

The mean change on the HOOS pain subscale was 8.6 (CI, 5.3 to 11.8) points in the PRT group and 9.3 (CI, 5.9 to 12.6) points in the NEMEX group (Table 2). The between-group difference was −0.7 (CI, −5.3 to 4.0) points, which was less than the trial-specific MID of 7.7 points. The mean change on the HOOS QoL subscale was 8.0 (CI, 4.3 to 11.7) points in the PRT group and 5.7 (CI, 1.9 to 9.5) points in the NEMEX group. The between-group difference was 2.3 (CI, −3.0 to 7.6) points, which was below the trial-specific MID of 8.4 points.

Table 2. Changes From Baseline to 12-Week Follow-up in Primary and Secondary Outcomes in the Intention-to-Treat Population*

Outcome	NEMEX ($n = 78$)			PRT ($n = 82$)			Difference in Change
	Baseline	12-Week Follow-up	Change	Baseline	12-Week Follow-up	Change	
Functional performance tests							
30-s chair stand test, *reps*†	11.6 (10.7 to 12.4)	13.1 (12.1 to 14.0)	1.5 (0.9 to 2.1)	11.3 (10.5 to 12.2)	12.8 (11.9 to 13.7)	1.5 (0.9 to 2.1)	0.0 (−0.8 to 0.8)
40-m fast-paced walk test, *s*‡	24.4 (23.0 to 26.0)	23.4 (22.0 to 24.9)	−4% (−2% to −6%)	24.9 (23.5 to 26.5)	23.8 (22.4 to 25.3)	−5% (−3% to −7%)	0% (−3% to 3%)
9-step timed stair climb test, *s*‡	10.4 (9.5 to 11.3)	9.5 (8.7 to 10.3)	−9% (−5% to −12%)	10.4 (9.5 to 11.3)	9.5 (8.7 to 10.3)	−9% (−5% to −12%)	0% (−5% to 5%)
Leg extensor power, *W/kg*							
Affected limb	1.67 (1.46 to 1.88)	1.85 (1.63 to 2.07)	0.18 (0.09 to 0.28)	1.50 (1.29 to 1.70)	1.75 (1.53 to 1.96)	0.25 (0.16 to 0.34)	0.07 (−0.07 to 0.20)
Unaffected/less affected limb	1.84 (1.60 to 2.09)	1.97 (1.73 to 2.21)	0.13 (0.03 to 0.22)	1.67 (1.43 to 1.91)	1.84 (1.61 to 2.08)	0.17 (0.08 to 0.26)	0.05 (−0.08 to 0.17)
Unilateral 1RM leg press, *kg*	71.0 (62.9 to 79.1)	82.9 (73.8 to 91.9)	11.9 (6.4 to 17.3)	68.2 (60.2 to 76.1)	84.2 (75.3 to 93.1)	16.0 (10.8 to 21.3)	4.2 (−3.4 to 11.7)
Patient-reported outcomes§							
HOOS pain‖	58.9 (54.8 to 62.9)	68.2 (63.8 to 72.5)	9.3 (5.9 to 12.6)	57.5 (53.6 to 61.6)	66.1 (61.9 to 70.4)	8.6 (5.3 to 11.8)	−0.7 (−5.3 to 4.0)
HOOS QoL‖	47.1 (43.1 to 51.1)	52.8 (48.3 to 57.3)	5.7 (1.9 to 9.5)	43.7 (39.8 to 47.6)	51.7 (47.3 to 56.0)	8.0 (4.3 to 11.7)	2.3 (−3.0 to 7.6)
HOOS ADL	64.7 (60.5 to 69.0)	73.8 (69.5 to 78.1)	9.1 (5.7 to 12.5)	63.4 (59.2 to 67.5)	70.9 (66.7 to 75.1)	7.5 (4.2 to 10.8)	−1.6 (−6.3 to 3.1)
HOOS sports/recreation	48.7 (43.4 to 54.0)	62.6 (57.0 to 68.3)	13.9 (9.0 to 18.8)	48.4 (43.2 to 53.5)	56.7 (51.2 to 62.2)	8.3 (3.6 to 13.1)	−5.5 (−12.3 to 1.2)
HOOS symptoms	57.7 (54.5 to 60.9)	62.2 (58.7 to 65.8)	4.5 (1.5 to 7.6)	54.9 (51.8 to 58.1)	61.3 (57.8 to 64.8)	6.4 (3.4 to 9.3)	1.8 (−2.4 to 6.1)

1RM = 1-repetition maximum; ADL = activities of daily living; HOOS = Hip Disability and Osteoarthritis Outcome Score; NEMEX = neuromuscular exercise; PRT = progressive resistance training; QoL = quality of life; reps = repetitions completed; W/kg = power output in watts normalized to body weight in kilograms.

* Results are presented as means (95% CIs) unless otherwise indicated. Intracluster correlation coefficients are shown in **Supplement Table 3** (available at Annals.org).

† Primary outcome measure.

‡ Assumptions for mixed-effects analysis were not met, so data were analyzed on a log scale. Results are presented as medians (95% CIs) for baseline and 12-week follow-up values; median ratios for changes and median ratios of ratios for differences are presented as percentages (95% CIs).

§ Scores on the HOOS range from 0 (worst) to 100 (best).

‖ Key secondary outcome measure.

Other Secondary Outcomes

There were no clinically relevant differences in changes in physical function, pain, or QoL (**Table 2**). The point estimates for between-group differences in mean improvement favored PRT for leg extensor muscle power in the affected limb (0.07 [CI, −0.07 to 0.20] W/kg) and the unaffected or less affected limb (0.05 [CI, −0.08 to 0.17] W/kg) and 1RM strength in the affected limb (4.2 [CI, −3.4 to 11.7] kg) and favored NEMEX for the HOOS sports/recreation subscale (−5.5 [CI, −12.3 to 1.2] points).

The number of participants reporting an important improvement in GPE after NEMEX or PRT was 39 (50%) and 43 (52%) for pain, 39 (50%) and 46 (56%) for ADL, and 38 (49%) and 46 (56%) for QoL, respectively. The number reporting an important deterioration was 4 (5%) and 7 (9%) for pain, 1 (1%) and 4 (5%) for ADL, and 1 (1%) and 5 (6%) for QoL, respectively.

Exercise Adherence and Fidelity

Mean adherence was 82% for PRT and 85% for NEMEX, and mean fidelity was 80% for PRT and 77% for NEMEX (**Table 3**). Mean exercise intensity for exercises in the PRT group for sessions 2, 8, 16, and 24 was 13 (CI, 11 to 14), 18 (CI, 16 to 20), 23 (CI, 21 to 25), and 27 (CI, 25 to 30) kg, respectively, and the mean number of repetitions per exercise was 36 (CI, 35 to 37), 36 (CI, 35 to 37), 31 (CI, 30 to 31), and 24 (CI, 24 to 25). The mean level of difficulty on a scale of 0 to 4 for exercises in the NEMEX group for sessions 2, 8, 16, and 24 was 1.5 (CI, 1.4 to 1.6), 2.4 (CI, 2.2 to 2.6), 2.8 (CI, 2.6 to 3.0), and 3.1 (CI, 2.9 to 3.3), respectively, and the mean number of repetitions per exercise was 57 (CI, 53 to 60), 63 (CI, 60 to 67), 64 (CI, 61 to 68), and 64 (CI, 59 to 68). Details on exercise variables are provided in **Supplement Figures 1** and **2** (available at Annals.org).

Adverse Events

At the 12-week follow-up, 3 serious adverse events were reported (2 in the PRT group and 1 in the NEMEX group), which were unrelated to or had a doubtful relationship with the interventions (**Table 3**). A total of 40 adverse events were reported (19 in the PRT group and 21 in the NEMEX group), with the most frequent

Table 3. Adverse Events, Dropouts, and Adherence to Interventions in the Intention-to-Treat Population at 12-Week Follow-up

Variable	NEMEX (*n* = 78)	PRT (*n* = 82)
Serious adverse events, *n (%)**	1 (1)	2 (2)
Umbilical hernia	0 (0)	1 (1)
Colon cancer	0 (0)	1 (1)
THA scheduled due to increase in hip pain	1 (1)	0 (0)
Adverse events, *n**	21	19
Increase in hip pain, *n (%)*	8 (10)	7 (9)
Knee pain, *n (%)*	9 (12)	4 (5)
Back pain, *n (%)*	1 (1)	1 (1)
Neck pain, *n (%)*	1 (1)	1 (1)
Hematoma on thigh, *n (%)*	0 (0)	1 (1)
Muscle soreness, *n (%)*	2 (3)	5 (6)
Dropouts, *n (%)*†	6 (8)	7 (9)
Mean adherence to group sessions, %	85	82
Participants with ≥80% adherence, *n (%)*	53 (68)	52 (63)
Participants with ≥50% adherence, *n (%)*	69 (88)	70 (85)
Mean proportion of sets completed, %‡	77	80
Participants with ≥80% fidelity, *n (%)*	38 (49)	50 (61)
Participants with ≥50% fidelity, *n (%)*	68 (87)	67 (82)
Joint replacements, *n (%)*	0 (0)	0 (0)

NEMEX = neuromuscular exercise; PRT = progressive resistance training; THA = total hip arthroplasty.

* Distinctions between adverse events and serious adverse events were made according to the guidelines from The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. Adverse events were reported by physiotherapists during interventions or outcome assessments. No more than 1 adverse event was reported for any participant. Data on serious adverse events include those that occurred between baseline and 12-week follow-up but did not necessarily have a causal relationship with the treatments.

† Defined as participants who did not complete the primary outcome at 12-week follow-up.

‡ The NEMEX program prescribes 2 or 3 sets for each exercise. Therefore, fidelity was calculated as the percentage of prescribed sets completed from a maximum of 2 sets for NEMEX and 3 for PRT.

being an increase in hip pain (7 in the PRT group and 8 in the NEMEX group), knee pain (4 in the PRT group and 9 in the NEMEX group), and muscle soreness (5 in the PRT group and 2 in the NEMEX group).

Per Protocol Analyses

The number of participants who had 80% adherence and 80% fidelity to the interventions and thus qualified for the per protocol PRT and NEMEX populations was 50 (61%) and 38 (49%), respectively (**Appendix Table 3**, available at Annals.org). Compared with the intention-to-treat populations, these participants achieved similar or slightly greater mean improvements. No clinically relevant between-group differences were found, indicating that the intention-to-treat results are robust.

Discussion

Changes from baseline to 12-week follow-up in 30s-CST, HOOS pain subscale score, and HOOS QoL subscale score did not support the hypothesis of superiority of PRT over NEMEX as there were no clinically relevant between-group differences. The between-group difference in the proportions of participants achieving the MaCII for the primary outcome or the MIC for key secondary outcomes did not reach the clinically relevant threshold of 20 percentage points (**Appendix Figure 3**, available at Annals.org).

The primary hypothesis was that PRT would result in greater improvements in functional performance than NEMEX through greater increases in muscle strength and power. However, the point estimates only showed modest and uncertain superiority of PRT for increasing muscle strength and power and no differences for any functional performance tests or self-reported physical function. The lack of superiority of PRT for increasing muscle strength and power is surprising given the principle of specificity (higher-intensity resistance training yields greater improvements in maximal muscle strength) (44). A possible explanation is that this study population was severely deconditioned, which could be attributed to only 40% to 41% of participants reporting at least 150 minutes of moderate-intensity physical activity per week compared with 63% of participants in a nationwide cohort of Danish patients with hip OA (45). Group means at baseline for the 30s-CST were 2.2 to 3.3 repetitions lower compared with a previous trial in a similar hip OA population not awaiting total hip arthroplasty (46). Consequently, the elastic bands and body weight exercises in NEMEX may have provided sufficient intensity to allow similar increases in mean relative muscle strength of 17% compared with 24% for PRT. These improvements are similar to reported improvements in 1RM leg press strength (16%) among healthy older adults after 11 weeks of PRT (27). Regarding muscle power of the more affected limb, the relative changes found for NEMEX (11%) and PRT (17%) were smaller than those previously reported by Hermann and colleagues (12) in patients with hip OA scheduled for total hip arthroplasty after a similar 12-week explosive-type PRT intervention (27%). However, this was an effectiveness trial under a real-world clinical setting, whereas the trial by Hermann and colleagues was a single-center efficacy trial under more ideal circumstances, which is believed to have influenced the magnitude of the effects (47).

The observed effects of PRT and NEMEX on physical function, pain, and QoL are similar in magnitude to those reported in previous exercise trials in hip OA that evaluated PRT, NEMEX, or Nordic walking (10, 12, 46). However, the mean changes in 30s-CST did not reach the MaCII of 2.6 chair stands defined by Wright and colleagues (33). As recommended by Terwee and colleagues (48), no MIC was estimated due to a low correlation between 30s-CST and GPE (Spearman correlation coefficient <0.3). Because PRT was not superior to NEMEX, patients and clinicians

may instead, through shared decision making, choose the preferred type of exercise, which will likely promote motivation, adherence, and effects (49). The slightly larger improvement in muscle strength and power after PRT may provide a reason for choosing PRT for patients who present with muscle weakness or are at risk for developing sarcopenia (50). Conversely, NEMEX can be a more practical and preferable choice for some patients and clinicians, and it might provide superior results for physical function in sports and recreational activities, requires minimal and inexpensive equipment, and can easily be performed at home.

Future trials should identify responders to exercise in hip OA and investigate the underlying mechanisms, which are largely unknown (51). High-quality trials exploring optimal content of exercise are also warranted. Of note, a randomized controlled trial found aerobic exercise delivered as Nordic walking to be superior to PRT and home-based exercise (46). However, high dropout rates and risk of differential dropout bias necessitate reproduction of this finding.

Several limitations of this trial should be noted. First, the physiotherapists delivering the interventions and the participants performing the exercises could not be blinded to treatment allocation. This could have introduced performance bias, as the physiotherapists and participants may have preferred one type of exercise and may have been more enthusiastic about supervising or performing those exercises. Second, the lack of a passive control group prevents claims about the clinical relevance of the effects of the individual interventions due to contextual factors and regression toward the mean. It is well established that placebo and contextual factors explain a large part of the effect of exercise and other treatments for OA (52, 53). However, given the proven clinical effectiveness (4), health benefits (54), and cost-effectiveness (55) of exercise, high-quality clinical practice guidelines consistently recommend it as first-line treatment for hip OA (56).

In conclusion, PRT is not superior to NEMEX for improving functional performance, hip pain, or hip-related QoL in patients with hip OA.

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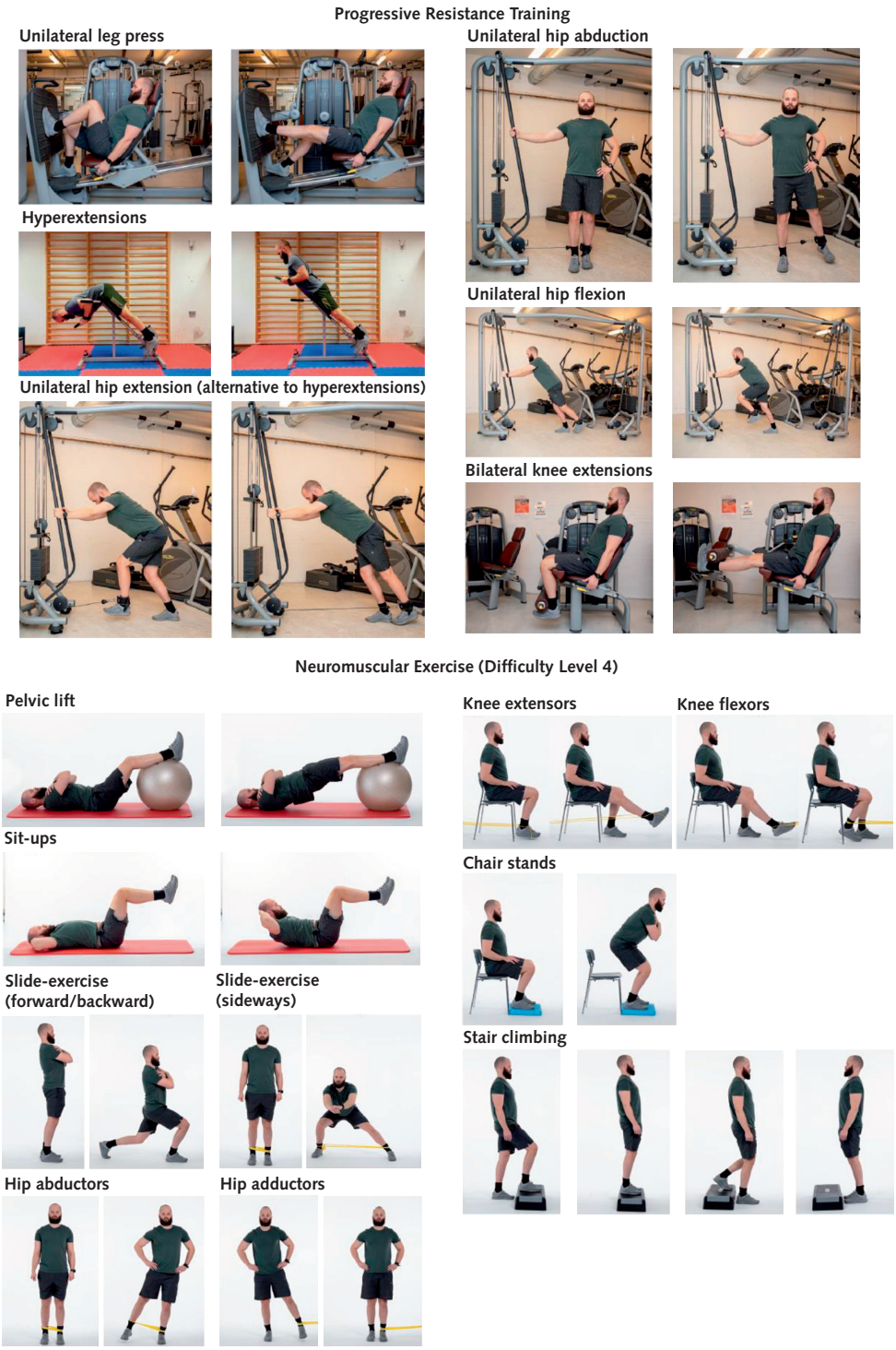
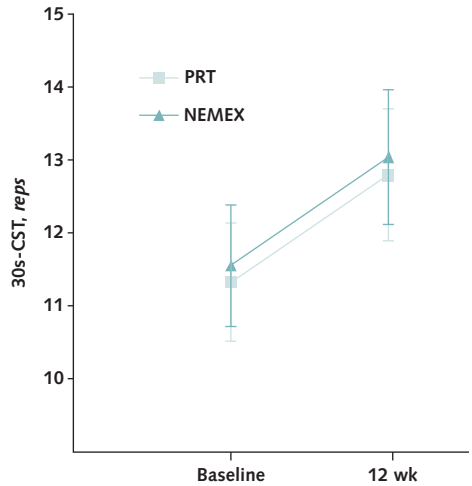
Appendix Figure 1. Exercises at starting position (left) and at end range of motion (right) for the 2 exercise interventions.



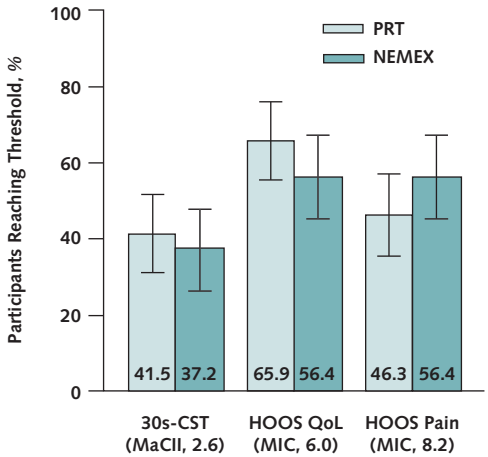
Only difficulty level 4 is shown for the neuromuscular exercises. Levels 1 to 3 can be found in a supplement to the article by Ageberg and colleagues (25). (Reproduced from *BMJ Open*, vol. 12, Kjeldsen T, Dalgas U, Skou ST, et al, Progressive resistance training compared to neuromuscular exercise in patients with hip osteoarthritis and the additive effect of exercise booster sessions: protocol for a multicentre cluster randomised controlled trial (The Hip Booster Trial), page pe061053, © Authors (or their employers) 2022, with permission. Reuse permitted under CC BY-NC.)

Appendix Figure 2. Changes in the primary outcome measure (30s-CST) after a 12-week intervention of PRT or NEMEX in patients with hip osteoarthritis.



30s-CST = 30-second chair stand test; NEMEX = neuromuscular exercise; PRT = progressive resistance training.

Appendix Figure 3. Proportion of participants in each treatment group attaining the MaCII in the primary outcome and MICs for key secondary outcomes after 12 weeks of PRT or NEMEX.



30s-CST = 30-second chair stand test; HOOS = Hip Disability and Osteoarthritis Outcome Score; MaCII = major clinically important improvement; MIC = minimal important change; NEMEX = neuromuscular exercise; PRT = progressive resistance training; QoL = quality of life.

Appendix Table 1. Descriptions of the PRT and NEMEX Interventions*

Exercise Type	PRT			NEMEX
Periodization model	Block 1 (weeks 1–4)	Block 2 (weeks 5–8)	Block 3 (weeks 9–12)	Exercise difficulty level is progressed linearly throughout the intervention
Volume, *reps/set*	12	10	8	10–15
Exercise intensity	12 RM	10 RM	8 RM	Not controlled for
Sets/exercise, *n*	3			2–3
Muscle contraction types				Every contraction phase is performed with maximal control, functional alignment, and a steady pace (1–3 s)
Concentric	As fast as possible			
Isometric	1 s			
Eccentric	3 s			
Time under tension, *s/rep*	4–6			Not controlled for
Time between repetitions, *s*	0			0
Time between sets, *s*	60			Equivalent to completing 1 set
Session duration, *m*	60			60
Sessions/week, *n*	2			2
Time between sessions, *h*	>72			>72
Supervised and group-based	Initial 12 wk			Initial 12 wk
Focus for exercises	Maximal intensity (exercise weight) and volume without compromising technique			Stability, postural function, postural orientation, lower extremity muscle strength, functional exercises
Range of motion	Full			Full
Volitional muscle failure	Third set only			Not controlled for
Order of adjusting exercises in case of pain exacerbation	Pace → range of motion → intensity			Pace → range of motion → number of repetitions → difficulty level
Progression	When able to perform all assigned repetitions in the third set, the weight is increased by 2%–10 %			When able to perform 15 repetitions for 3 sets with good sensorimotor control, movement quality, and acceptable exertion, progression is made to the next level of difficulty
Equipment	Leg press machine, knee extension machine, hyperextension bench, dumbbells, cable pulley, ankle straps			Aerobic stepper, Pilates exercise ball, elastic bands, sliding mat, chair with armrest, foam balance pad

NEMEX = neuromuscular exercise; PRT = progressive resistance training; reps = repetitions; RM = repetition maximum.
* Reproduced from *BMJ Open*, vol. 12, Kjeldsen T, Dalgas U, Skou ST, et al, Progressive resistance training compared to neuromuscular exercise in patients with hip osteoarthritis and the additive effect of exercise booster sessions: protocol for a multicentre cluster randomised controlled trial (The Hip Booster Trial), page pe061053, © Authors (or their employers) 2022, with permission. Reuse permitted under CC BY-NC.

Appendix Table 2. Sensitivity Analyses on Changes From Baseline to 12-Week Follow-up in Primary and Key Secondary Outcomes in the Intention-to-Treat Population With Recruitment Site (Hospital or Clinic) Included as a Fixed Effect in the Mixed-Effects Model*

Outcome	NEMEX (*n* = 78)			PRT (*n* = 82)			Difference in Change
	Baseline	12-Week Follow-up	Change	Baseline	12-Week Follow-up	Change	
30-s chair stand test, *reps*	11.7 (10.8 to 12.5)	13.2 (12.2 to 14.1)	1.5 (0.9 to 2.1)	11.2 (10.4 to 12.1)	12.7 (11.8 to 13.7)	1.5 (0.9 to 2.1)	0.0 (−0.8 to 0.8)
HOOS pain†	59.8 (55.6 to 64.0)	69.0 (64.5 to 73.5)	9.2 (5.9 to 12.6)	56.9 (52.8 to 61.0)	65.4 (61.0 to 69.8)	8.5 (5.3 to 11.8)	−0.7 (−5.3 to 4.0)
HOOS QoL†	47.8 (43.7 to 51.9)	53.5 (48.9 to 58.0)	5.6 (1.8 to 9.4)	43.1 (39.1 to 47.1)	51.1 (46.7 to 55.5)	7.9 (4.3 to 11.6)	2.3 (−3.0 to 7.6)

HOOS = Hip Disability and Osteoarthritis Outcome Score; NEMEX = neuromuscular exercise; PRT = progressive resistance training; QoL = quality of life; reps = repetitions completed.
* Results are presented as means (95% CIs).
† Scores on the HOOS range from 0 (worst) to 100 (best).

Appendix Table 3. Changes From Baseline to 12-Week Follow-up in Primary and Secondary Outcomes in the Per Protocol Population That Included Only Participants With ≥80% Adherence to Sessions and ≥80% Fidelity to the Exercise Program*

Outcome	NEMEX ($n = 38$)			PRT ($n = 50$)			Difference in Change	Adjusted Difference in Change†
	Baseline	12-Week Follow-up	Change	Baseline	12-Week Follow-up	Change		
Functional performance tests								
30-s chair stand test, *reps*‡	12.1 (10.9 to 13.2)	14.2 (12.9 to 15.6)	2.2 (1.3 to 3.0)	11.5 (10.5 to 12.6)	12.8 (11.7 to 14.0)	1.3 (0.5 to 2.0)	−0.9 (−2.0 to 0.3)	−0.9 (−2.0 to 0.2)
40-m fast-paced walk test, *s*§	23.2 (21.8 to 24.8)	22.2 (20.8 to 23.7)	−4% (−2% to −7%)	24.2 (22.8 to 25.7)	22.9 (21.6 to 24.2)	−6% (−3% to −8%)	1% (−2% to 5%)	1% (−2% to 4%)
9-step timed stair climb test, *s*§	9.9 (9.0 to 10.8)	8.8 (8.1 to 9.6)	−10% (−6% to −15%)	9.8 (9.1 to 10.6)	9.1 (8.5 to 9.8)	−7% (−3% to −11%)	−4% (−11% to 3%)	−5% (−11% to 1%)
Leg extensor power, *W/kg*								
Affected limb	1.72 (1.47 to 1.97)	2.00 (1.74 to 2.25)	0.28 (0.14 to 0.41)	1.52 (1.29 to 1.75)	1.80 (1.56 to 2.03)	0.27 (0.16 to 0.39)	0.00 (−0.18 to 0.17)	−0.02 (−0.18 to 0.13)
Unaffected/less affected limb	1.90 (1.64 to 2.16)	2.12 (1.87 to 2.36)	0.21 (0.08 to 0.34)	1.74 (1.50 to 1.98)	1.90 (1.67 to 2.13)	0.16 (0.05 to 0.27)	−0.05 (−0.22 to 0.12)	−0.08 (−0.24 to 0.07)
Unilateral 1RM leg press, *kg*	72.1 (60.7 to 83.4)	87.3 (74.8 to 99.8)	15.3 (7.7 to 22.8)	69.6 (59.2 to 80.1)	89.8 (78.4 to 101.1)	20.1 (13.7 to 26.5)	4.9 (−5.0 to 14.7)	5.1 (−4.1 to 14.4)
Patient-reported outcomes‖								
HOOS pain¶	61.0 (56.0 to 66.0)	73.9 (68.3 to 79.5)	12.9 (7.9 to 17.9)	59.3 (54.8 to 63.8)	68.3 (63.3 to 73.3)	9.0 (4.7 to 13.3)	−3.9 (−10.5 to 2.7)	−4.7 (−10.3 to 0.9)
HOOS QoL¶	48.2 (43.1 to 53.4)	58.1 (52.1 to 64.1)	9.9 (4.6 to 15.2)	43.8 (39.2 to 48.3)	53.3 (48.0 to 58.6)	9.5 (5.0 to 14.0)	−0.4 (−7.4 to 6.6)	−0.6 (−6.8 to 5.7)
HOOS ADL	66.5 (61.0 to 72.0)	79.0 (73.7 to 84.2)	12.4 (7.4 to 17.5)	64.0 (59.2 to 68.9)	74.0 (69.3 to 78.6)	9.9 (5.6 to 14.2)	−2.5 (−9.2 to 4.1)	−4.3 (−10.9 to 1.9)
HOOS sports/recreation	47.4 (40.2 to 54.5)	67.0 (59.4 to 74.5)	19.6 (13.1 to 26.0)	50.0 (43.7 to 56.2)	58.1 (51.5 to 64.7)	8.1 (2.6 to 13.6)	−11.4 (−19.9 to −3.0)	−11.6 (−19.5 to −3.8)
HOOS symptoms	58.6 (54.5 to 62.7)	66.5 (61.7 to 71.3)	7.9 (3.6 to 12.1)	55.0 (51.4 to 58.7)	62.6 (58.4 to 66.8)	7.6 (4.0 to 11.2)	−0.3 (−5.9 to 5.3)	−0.5 (−5.4 to 4.5)

1RM = 1-repetition maximum; ADL = activities of daily living; HOOS = Hip Disability and Osteoarthritis Outcome Score; NEMEX = neuromuscular exercise; PRT = progressive resistance training; QoL = quality of life; reps = repetitions completed; W/kg = power output in watts normalized to body weight in kilograms.

* Results are presented as means (95% CIs) unless otherwise indicated.

† Adjusted differences in change were estimated using inverse probability–weighted regression adjustment analyses due to the potential influence of bias in per protocol analyses where factors that influence adherence can also be related to the outcomes. The prognostic factors included in these adjusted analyses were age, sex, body mass index, duration of symptoms, comorbidities, use of analgesics, and prior exercise therapy.

‡ Primary outcome measure.

§ Assumptions for mixed-effects analysis were not met, so data were analyzed on a log scale. Results are presented as medians (95% CIs) for baseline and 12-week follow-up values; median ratios for changes and median ratios of ratios for differences are presented as percentages (95% CIs).

‖ Scores on the HOOS range from 0 (worst) to 100 (best).

¶ Key secondary outcome measure.