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Neuromuscular Control and Resistance Training for People With Chronic Low Back Pain: A Randomized Controlled Trial

OBJECTIVE: To determine if adding lumbar neuromuscular control retraining exercises to a 12-week program of strengthening exercises had greater effect for improving disability than 12 weeks of strengthening exercises alone in people with chronic low back pain (LBP).

DESIGN: Single-center, participant- and assessor-blinded, comparative effectiveness randomized controlled trial.

METHODS: Sixty-nine participants (31 females; 29 males; mean age: 46.5 years) with nonspecific chronic LBP were recruited for a 12-week program involving lumbar extension neuromuscular retraining in addition to resistance exercises (intervention) or 12 weeks of resistance exercises alone (control). The primary outcome measure was the Oswestry Disability Index. Secondary outcome measures included the Numeric Rating Scale, Tampa Scale for Kinesiophobia, Pain Self-Efficacy Questionnaire, and the International Physical Activity Questionnaire. Outcomes were measured at baseline, 6 weeks, and 12 weeks.

RESULTS: Forty-three participants (22 control, 21 intervention) completed all outcome measures at 6 and 12 weeks. Fourteen participants were lost to follow-up, and 12 participants discontinued due to COVID-19 restrictions. Both groups demonstrated clinically important changes in disability, pain intensity, and kinesiophobia. The difference between groups with respect to disability was imprecise and not clinically meaningful (mean difference, −4.4; 95% CI: −10.2, 1.4) at 12 weeks. Differences in secondary outcomes at 6 or 12 weeks were also small with wide confidence intervals.

CONCLUSIONS: Adding lumbar neuromuscular control retraining to a series of resistance exercises offered no additional benefit over resistance exercises alone over a 12-week period. *J Orthop Sports Phys Ther 2024;54(5):350-359. Epub 18 March 2024. doi:10.2519/jospt.2024.12349*

KEY WORDS: *low back pain, randomized controlled trial, rehabilitation exercise, resistance training, spine*

Chronic low back pain (CLBP) is a complex multifactorial condition[32] reducing the quality of life of millions of people around the world.[21,24] In addition to pain, patients are physically limited[46] and psychologically impacted.[28,38] Exercise interventions, such as resistance training, are effective for treating CLBP.[49,56] However various exercise interventions focusing on physical impairments including weakness, fatigue, and reduced activation of lumbar muscles[32] have no superiority over one another.[25] A lack of clinically important differences between exercise interventions may be related to poor associations between physical impairments and CLBP-related disability or function, and the positive impact of exercise on multiple factors such as fear-avoidance beliefs and muscle strength[12,55] associated with CLBP-related disability.

Neuromuscular deficits of the trunk muscles have been described in the CLBP literature for over 30 years.[26] Like other interventions focusing on physical impairments, interventions targeting *neuromuscular deficits* have not yielded superior results to other exercise interventions.[47] A criticism of the neuromuscular deficits investigated to date is that they lack translation to functional impairments in people with CLBP. A newly identified impairment in lumbar extension neuromuscular control (ie, ability to control the force produced into lumbar extension) has demonstrated a relationship with self-reported disability in people with CLBP.[43] A cross-sectional study reported a relationship between CLBP-related lifting dysfunction and lumbar extensor neuromuscular control deficits.[44] It may be important to establish whether retraining lumbar extensor neuromuscular control in combination with resistance exercises yields greater improvements in CLBP-related disability compared to previously investigated strengthening exercises alone. Therefore, the primary research question was as follows:

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Is the addition of lumbar neuromuscular control retraining exercises to a 12-week program of strengthening exercises more efficacious for improving disability compared with 12 weeks of strengthening exercises alone in people with CLBP? It was hypothesized that CLBP participants receiving neuromuscular control exercise targeted at improving lumbar extensor neuromuscular control in addition to resistance exercise would demonstrate a greater reduction in self-reported disability compared to those only receiving resistance exercises at 12 weeks.

METHODS

Study Design

We conducted a 2-arm, parallel group, participant- and assessor-blinded, comparative randomized controlled trial (RCT). The protocol has been published.[17] The trial was prospectively registered with the Australian New Zealand Clinical Trials Registry (ACTRN12618000894291) and was approved by The University of Melbourne's Behavioural and Social Sciences Human Ethics Sub-Committee (reference number 1749845).

Participants were randomly assigned to groups (neuromuscular [NM] group or the strengthening [ST] group) in permuted blocks of 6 to 12 stratified by baseline Oswestry Disability Index (ODI) level (moderate or severe/greater) (**FIGURE**). The randomization schedule was prepared by an independent researcher. The schedule was stored on a password-protected website (REDCap, Vanderbilt University) and maintained by an off-site researcher not involved in enrolment or outcome assessment. Participants completed primary, secondary, and additional outcomes at baseline, 6 weeks, and 12 weeks. Participants and assessors were blinded to group allocation during collection and analysis of all outcome measures. The interventions were designed to use identical exercise equipment to make it more difficult for participants to determine which group they were in. Participants recorded which group they believed they were allocated to and were able to indicate if they were unsure (after the 12-week assessment or after withdrawing from the trial); they were also asked whether the therapist revealed their allocation at any time throughout the trial. The James Blinding Index was used to assess the success of blinding.[29] The assessor was not involved in the randomization or intervention and was therefore blinded to participant group allocation. In addition, the biostatistician involved in statistical analysis of the data was blinded. The

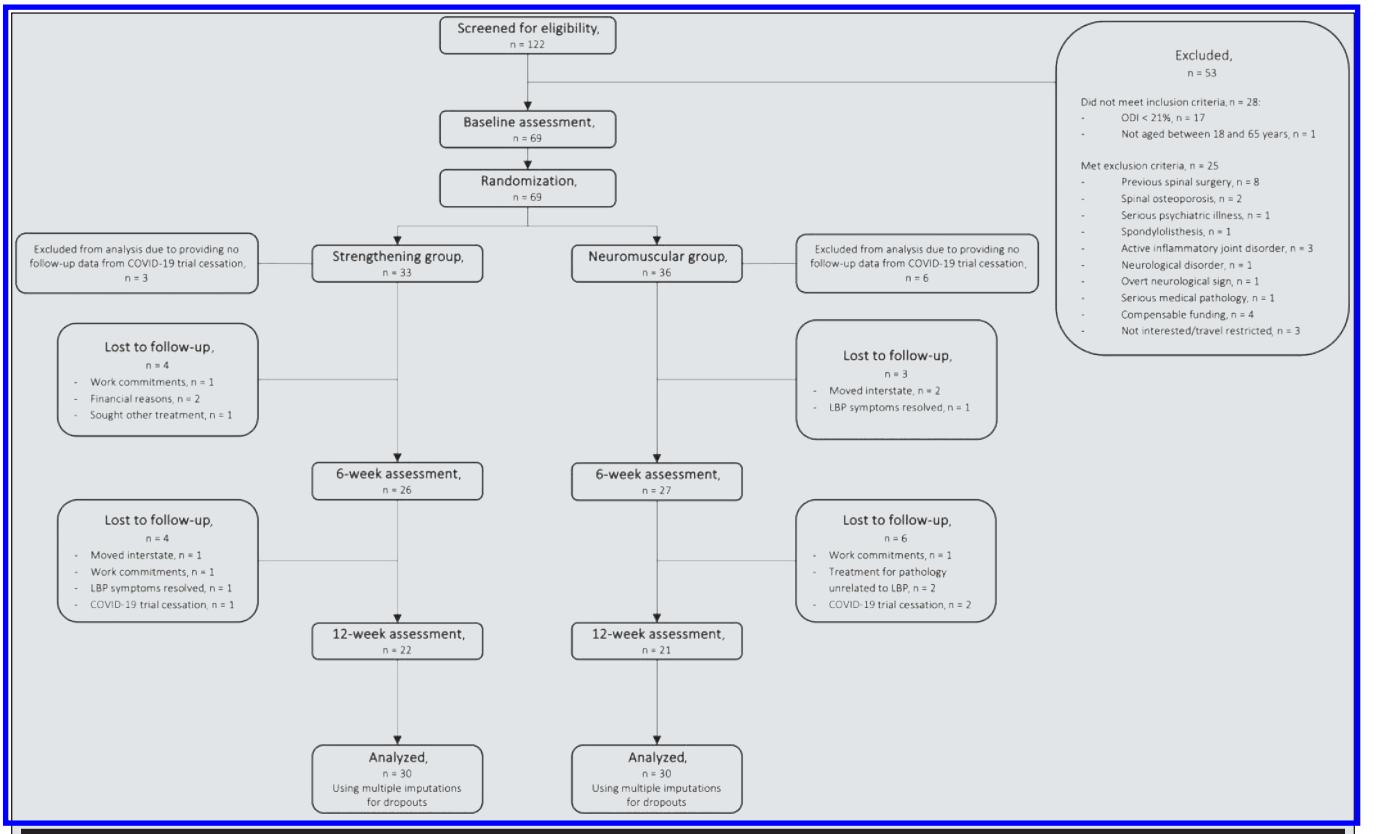

FIGURE. Study flow diagram. Abbreviations: LBP, low back pain, NSCLBP, nonspecific chronic low back pain; ODI, Oswestry Disability Index.

Consolidated Standards of Reporting Trials (CONSORT) statement[48] was used in the reporting of this RCT.

Participants

We recruited 69 participants with CLBP from a physiotherapy clinic in Melbourne, Australia from July 2018 until March 2020. Informed consent was obtained from all participants and the rights of the participants were protected. The study was terminated prematurely in March 2020 due to COVID-19 restrictions imposed by the Victorian State Government. Male and female participants were included if they were aged between 18 and 65 years, had LBP (with or without lower limb pain) for at least 3 months, and demonstrated moderate or higher disability on the ODI (ie, 21% or higher).[16] Exclusion criteria were previous spinal or lower-limb surgery, spinal osteoporosis or osteopenia, spondylolisthesis or spondylosis, medication-managed psychological illness, neurological or developmental disorder, overt neurological sign, significant medical condition (eg, cancerous pathology), use of medication that affected balance, abdo-pelvic organ prolapse, funding by a compensable body, pregnant or up to 6 months postpartum, and an inability to understand English.

Intervention

Participants from both groups undertook 24 exercise sessions over 12 weeks (2 per week) supervised by physiotherapists with 1 to 10 years of clinical experience. Each exercise session lasted ~30 minutes. All physiotherapists were trained to deliver the protocol by the primary researcher who developed the protocol. During each session, all participants (both groups) completed resistance training involving a lumbar extension resistance exercise as well as at least one other resistance exercise of either leg press, trunk flexion, or hip extension; the decision as to which other exercise(s) were completed was made by the physiotherapist based on their clinical recommendation for each participant. Participants completed a maximum voluntary isometric contraction (MVIC) for each exercise used in the study. The starting weight for each resistance exercise was set at 85% of the MVIC. Each exercise was performed repetitively over a 2-minute period or until fatigue.[17] This resistance training protocol conforms to the current American College of Sports Medicine guidelines.[20]

In addition to the aforementioned resistance exercises, the intervention group completed a lumbar extension neuromuscular control retraining exercise at the beginning of each training session. Participants were seated in a MedX dynamometer (MedX, Ocala, FL), and with visual feedback, isometrically pressed their back against the backrest attempting to match a sinusoidal target force varying between 20% to 50% of their lumbar extension MVIC. This exercise was completed 3 times each session at 3 different frequencies (0.05 Hz, 0.08 Hz, and 0.14 Hz). The progression of this exercise is outlined in **SUPPLEMENTAL APPENDIX 1**. To control for the additional work performed by the intervention group, participants in the control group completed additional time on the lumbar extension resistance exercise at 50% of their MVIC. This was equivalent to the time participants in the experimental group spent on the neuromuscular exercise. The exercise interventions detailed in the protocol study were reported using the Template for Intervention Description and Replication (TIDieR) checklist.[27]

Outcome Measures

The primary outcome of disability was measured via the ODI, which is valid and reliable in a CLBP population.[14] Patient-reported outcomes were all completed electronically.

The secondary outcome measures were all valid and reliable for the measures of pain intensity,[30,41] kinesiophobia,[22,45] pain self-efficacy,[6,33] and physical activity.[10] Outcomes were measured via an 11-point Numeric Rating Scale (NRS),[7] 17-item Tampa Scale for Kinesiophobia (TSK-17),[34] Pain Self-Efficacy Questionnaire (PSEQ),[36] and the International Physical Activity Questionnaire - Short Form (IPAQ-SF)[2] as detailed in the protocol.[17] Patient-reported outcome measures were administered via an online database (REDCap). Additional outcome measures were used to investigate potential neuromuscular changes. These measures included lumbar extension strength; lumbar extensor force-matching error; average lifting time; maximum range of motion of the knee, hip, and lumbar spine during lifting; symmetry of weight-bearing during lifting; and lumbar multifidus thickness. Detailed descriptions of these outcome measures and how the measures were performed are reported in the published protocol.[17]

Adverse events of treatment were recorded electronically by the treating therapist. Cointerventions were recorded at 12 weeks by the assessor. Fidelity checking to review adherence to the protocol was assessed every 3 months by an independent and blinded clinician, who was not involved in assessment or treatment of the participants in the study.

Data Analysis

Analyses were performed by a blinded biostatistician using Stata version 16 (StataCorp, College Station, TX). An intention-to-treat analysis was used where the outcomes of participants were analyzed according to their randomized group. Baseline characteristics in each group were described using means and standard deviations, medians, and interquartile ranges, or numbers and percentages as appropriate. Cointervention use in each group over the course of the trial were described using numbers and percentages and compared using chi-squared tests.

Missing values were imputed using chained equations with predictive mean matching and 5 nearest neighbors.[57] Data were imputed for each randomized group separately. All primary and secondary outcomes were imputed together in the same model that included all baseline variables. The additional outcomes were each imputed in separate models that

also included all baseline variables and the outcome at both timepoints, but no other imputed variables. Estimates from 30 imputed datasets were combined using Rubin's rules.[4] An additional analysis was conducted in which data from all participants, including those who could not provide any follow-up data due to cessation of the trial, was imputed in the same manner as described above.

For all outcomes, mean differences in change (follow-up minus baseline) between groups were estimated at each timepoint using longitudinal linear mixed-effects models. These models included all data from 6 and 12 weeks as outcomes for each participant. They had an interaction between week and randomized group included as fixed effects, and random intercepts included for participants. All models were adjusted for baseline values of the outcome and the stratification variable of ODI score, dichotomized into moderate (21% to 40%) and severe disability (≥41%). Model assumptions and validity of imputed datasets were assessed using standard diagnostic plots.

The aim was to detect a 20% difference in ODI scores, which corresponds to the minimal clinically important difference (MCID).[39] With a standard deviation (SD) of 15, this difference corresponds to an effect size of 0.67, and the between-group ODI MCID can be detected with 80% power and a significance level of 0.05 with 37 participants per group. Allowing for 20% drop out, our aim was to recruit 47 participants to each group.

RESULTS

Sixty-nine participants were enrolled. Nine participants were unable to provide any follow-up measurements because of early cessation of the trial due to the COVID-19 pandemic. Baseline characteristics of these 9 participants were compared to the others in the trial, and given there were no clinically meaningful differences, they were not included in the primary analysis (**SUPPLEMENTAL APPENDIX 2**). The treatment effect being estimated in this analysis can be thought of as that which would describe the effect of the treatment had the COVID-19 pandemic not occurred;[11] hence, we have an effective sample size of 30 per group.

Treatment groups were similar at baseline (**TABLE 1**). Prior to the 6-week assessment, 7 participants (NM group = 3, ST group = 4) were lost to follow-up and between the 6- and 12-week assessment, a further 10 participants (NM group = 6, ST group = 4) respectively did not complete the primary outcome measure (**FIGURE**); three of the participants who did not complete the primary outcome at 12 weeks (NM group = 2, ST group = 1) were discontinued due to the COVID-19 restrictions after providing outcome data at 6 weeks.

All 60 participants analyzed received the intervention they were allocated to. Cointervention use was similar between groups with only manual therapy being used significantly more by participants in the strength group (**TABLE 2**). Seventeen participants did not provide information about cointervention use as they were lost to follow-up and did not complete the 12-week assessment. There was no significant difference in the use of manual therapy between responders (participants whose ODI improved greater than or equal to 20%) and nonresponders (participants whose ODI improved less than 20%) for either group (**SUPPLEMENTAL APPENDIX 3**). No adverse events occurred throughout the trial in either group. Most participants (83%) were unsure of their group allocation and of the 11 participants who indicated which group they believed they were in, eight were incorrect (**SUPPLEMENTAL APPENDIX 4**). A James Blinding Index of 0.95 (95% CI: 0.91, 0.99)

TABLE 1 Baseline Characteristics of Participants by Group, Reported as Number (Percentage) Unless Otherwise Stated

Characteristics	ST Group (n = 30)	NM Group (n = 30)
Sex		
Female	14 (47%)	17 (57%)
Male	16 (53%)	13 (43%)
Age (years), median (IQR)	46.5 (40-57)	51.5 (40-56)
Height (cm), mean (SD)	174.8 (10.8)	173.2 (9.4)
Mass (kg), median (IQR)	78.0 (66.1-96.0)	80.5 (68.9-84.9)
BMI (kg/m^2), median (IQR)	25.1 (22.3-29.2)	25.3 (22.9-28.7)
Duration of low back pain (months), median (IQR)	28.0 (11-110)	25.0 (9.0-60.0)
Manual therapy (ie, massage, manipulation)	23 (77%)	28 (93%)
Acupuncture or dry needling	9 (30%)	12 (40%)
Shock wave therapy	0 (0%)	0 (0%)
Ultrasound or TENS therapy	1 (3%)	2 (7%)
Cortisone injection	1 (3%)	4 (13%)
Nonsteroidal anti-inflammatories (eg, ibuprofen, meloxicam, celecoxib, diclofenac, acetylsalicylic acid, etc)	25 (83%)	24 (80%)
Corticosteroids (eg, prednisone, prednisolone, hydrocortisone, cortisone, dexamethasone, methylprednisolone)	4 (13%)	2 (7%)
Paracetamol	21 (70%)	24 (80%)
Tramadol	1 (3%)	1 (3%)
Oxycodone-based medications (eg, oxycodone with naloxone, oxycodone hydrochloride)	3 (10%)	1 (3%)
Codeine-based medications (eg, ibuprofen with codeine)	6 (20%)	6 (20%)

Abbreviations: BMI, body mass index; IQR, interquartile range; NM, neuromuscular; SD, standard deviation; ST, strengthening; TENS, transcutaneous electrical nerve stimulation.

TABLE 2 Cointervention Use of Participants Over the Course of the Trial, by Group, Reported as Number (Percentage)

Cointervention	ST Group (n = 30)	NM Group (n = 30)	*P* Value
Manual therapy (ie, massage, mobilization, manipulation)	19 (86%)	11 (52%)	0.02
Acupuncture or dry needling	4 (18%)	1 (5%)	0.17
Shock wave therapy	0 (0%)	0 (0%)	
Ultrasound or TENS therapy	1 (5%)	2 (10%)	0.52
Cortisone injection	1 (5%)	0 (0%)	0.32
Nonsteroidal anti-inflammatories (eg, ibuprofen, meloxicam, celecoxib, diclofenac, acetylsalicylic acid, etc)	14 (64%)	12 (57%)	0.66
Corticosteroids (eg, prednisone, prednisolone, hydrocortisone, cortisone, dexamethasone, methylprednisolone)	0 (0%)	0 (0%)	
Paracetamol	9 (41%)	12 (57%)	0.29
Tramadol	0 (0%)	0 (0%)	
Oxycodone-based medications (eg, oxycodone with naloxone, oxycodone hydrochloride)	0 (0%)	1 (5%)	0.30
Codeine-based medications (eg, ibuprofen with codeine)	3 (14%)	4 (19%)	0.63

Abbreviations: NM, neuromuscular; ST, strengthening; TENS, transcutaneous electrical nerve stimulation.

indicates successful participant blinding. Furthermore, no participants indicated they were unblinded by the therapist.

TABLE 3 summarizes continuous outcomes across time by groups. Differences in change between groups are shown in **TABLE 4**. For the primary outcome at 6 and 12 weeks, the estimate of the effect of between groups was consistent with no additional benefit in self-reported disability, it was also consistent with an additional benefit (mean change at 6 weeks: −2.25 units [95% CI: −7.19, 2.69] and mean change at 12 weeks: −4.39 units [95% CI: −10.19, 1.41], respectively). The sensitivity analysis, in which data were imputed from all participants, including the nine that could not provide any follow-up data due to the cessation of the trial, yielded similar results (**SUPPLEMENTAL APPENDIX 5**).

Between-group differences were small for secondary outcomes at both time points (**TABLE 4**). The sensitivity analysis yielded similar results (**SUPPLEMENTAL APPENDIX 5**). Although the estimate of the difference in force-matching error was in favor of the intervention group at the 6-week assessment, with a narrow confidence interval, the between-group difference in force-matching error at 12 weeks was small. There was no clinically meaningful between-group difference for any other additional outcome at any time.

DISCUSSION

Both 12-week exercise interventions resulted in clinically meaningful improvements in CLBP-related disability, pain intensity, and kinesiophobia. However, adding lumbar neuromuscular exercises to a program of strengthening exercises failed to improve self-reported disability more than strengthening exercises alone. As per the protocol paper,[17] the secondary objective of this study was to investigate the neuromuscular, biomechanical, and psychosocial mechanisms in which neuromuscular control retraining and resistance training may influence CLBP-related disability. Unfortunately, due to the COVID-19 pandemic, this study had to be prematurely ceased, and as such, we were not sufficiently powered to conduct analyses relating to the influence of neuromuscular or biomechanical factors on CLBP-related disability.

Given the novelty of the neuromuscular retraining intervention used in this study, there is no previous research to compare our findings. While there is evidence comparing isolated neuromuscular interventions to numerous other exercises and therapies, to our knowledge, no prior study has combined neuromuscular and resistance training as an intervention for people with CLBP. Previous research investigating lumbar extension neuromuscular control deficits that used a similar assessment protocol to this study identified a statistically significant difference between healthy controls and those with CLBP.[43]

Deficits in lumbar extensor neuromuscular control were associated with self-reported disability in people with CLBP.[43] Significantly, superior improvements in lumbar extension force-matching at 6 weeks favored the intervention group, although no greater improvements in any other outcome were observed. At 12 weeks, improvements in force-matching were similar between groups, suggesting that resistance training can augment similar improvements over a greater time period. In light of the findings of the aforementioned cross-sectional study,[43] it is unclear why the lumbar extension neuromuscular control retraining did not translate to improvements in disability over the control intervention. Potentially, CLBP-related disability may not be as significantly influenced by neuromuscular-biomechanical factors as the literature suggests.

Participant numbers did not allow within-group analysis of outcome measures, and as such, within-group comparisons were observational and not statistical. Both neuromuscular control retraining and resistance training resulted in large improvements in self-reported disability that exceeded the MCID of 10 units (20%) on the ODI,[39] resulting in a 22.3% and 25.9% reduction in disability at 12 weeks, respectively. Pain reductions, improvements in kinesiophobia and pain self-efficacy were also clinically relevant, surpassing the MCIDs of 2,[52] 6,[35] and 5.5 points,[8] respectively. At 12 weeks, large

TABLE 3 Continuous Outcomes Across Time, by Group, Reported as Mean (SD)

	Baseline		6 weeks		12 weeks	
	ST Group	NM Group	ST Group[a]	NM Group[b]	ST Group[c]	NM Group[d]
Primary Outcome						
Oswestry Disability Index (ODI %)	36.9 (12.7)	38.1 (8.8)	17.6 (11.4)	20.3 (9.6)	11.0 (6.2)	15.8 (12.1)
Secondary Outcomes						
Pain intensity (NRS)	5.1 (1.8)	5.8 (1.6)	3.7 (2.1)	4.1 (2.1)	2.5 (1.8)	2.7 (2.2)
Tampa Scale for Kinesiophobia (TSK-17)	38.0 (6.6)	38.0 (8.3)	33.2 (6.0)	33.7 (10.0)	29.7 (6.4)	31.1 (9.7)
Pain Self-Efficacy Questionnaire (PSEQ)	45.3 (9.4)	42.6 (11.2)	49.7 (8.0)	47.6 (10.8)	53.3 (6.7)	49.9 (10.1)
International Physical Activity Questionnaire - Short Form (IPAQ-SF) (METs)	3381 (4797)	2897 (1945)	4805 (7085)	2841 (2083)	3295 (1947)	3650 (3409)
Additional Outcomes						
Lumbar extension strength (N·m)	130.7 (64.5)	92.5 (52.8)	153.1 (92.0)	115.8 (67.8)	200.8 (113.6)	155.3 (81.5)
Force matching error	9.1 (9.0)	7.6 (5.1)	7.0 (5.0)	3.9 (1.2)	3.9 (1.3)	3.3 (1.6)
Average lifting time (s)	4.2 (0.8)	4.4 (1.3)	4.2 (1.5)	3.8 (0.8)	3.4 (0.6)	3.2 (0.6)
Max knee ROM during lifting (°)	76.8 (29.0)	67.8 (30.8)	79.5 (25.1)	68.7 (29.2)	79.2 (27.2)	66.1 (26.0)
Max hip ROM during lifting (°)	101.7 (14.8)	102.1 (17.9)	104.0 (11.6)	101.8 (16.6)	105.7 (11.4)	107.8 (10.2)
Max lumbar ROM during lifting (°)	43.3 (11.1)	40.4 (13.6)	42.1 (9.5)	42.0 (12.2)	40.4 (10.2)	37.2 (11.0)
Asymmetric WB mean during lifting (kg)	−0.5 (4.3)	−0.7 (4.7)	−0.8 (4.5)	−1.9 (3.9)	−1.2 (4.5)	−3.2 (3.8)
Asymmetric WB SD during lifting (kg)	7.2 (2.5)	7.8 (2.8)	8.5 (4.2)	8.5 (2.9)	8.2 (2.7)	9.0 (3.4)
LM thickness (cm)	2.5 (0.4)	2.6 (0.5)	2.7 (0.3)	2.7 (0.4)	2.8 (0.4)	2.9 (0.5)

Abbreviations: CI, confidence interval; LM, lumbar multifidus; METs, metabolic equivalents; NM, neuromuscular; NRS, Numeric Rating Scale; ROM, range of motion; SD, standard deviation; ST, strengthening; WB, weight-bearing.
[a] *n = 26.*
[b] *n = 27.*
[c] *n = 22.*
[d] *n = 21 before imputation.*

improvements in lumbar extension strength and reductions in force matching error were apparent for both groups, as well as decreases in average lifting time. However, there is no existing evidence from which to calculate an MCID for these outcomes. We are unable to determine the clinical significance of these improvements. Natural recovery is unlikely to explain our findings, given the participants' long-standing symptoms.

Underlying Mechanisms of Intervention Effects

A decline in disability levels for both exercise-based interventions may be related to both biomechanical and nonbiomechanical mechanisms. The benefits of exercise are multifactorial.[12,55] Participants from both groups displayed positive changes in kinesiophobia and pain self-efficacy, both of which have been associated with self-reported disability.[18,23] Thus, changes in nonbiomechanical outcomes may have influenced the decrease in ODI scores across both groups. However, the interrelationships between multiple mechanisms and how these contribute to CLBP-related disability is unclear.

Improvements in physical outcomes (eg, strength) may have contributed to improvements in self-confidence around the ability to move and cope with pain,[53] and vice versa. Exercise has analgesic effects for people with chronic pain. While a single bout of exercise can increase pain,[13] regular exercise can result in systemic hypoalgesia[31] via effects to the immune and central nervous systems.[42,51] Considering the close relationship between pain and disability in CLBP,[32] it is possible that hypoalgesia contributed to improvements in disability.

Greater use of manual therapy by participants in the strengthening group may have impacted disability and pain-related outcomes and contributed to the nonsignificant difference between groups. The lack of statistical power precluded further between-group (strengthening and neuromuscular groups) analysis to explore this notion. However, the proportion of responders and nonresponders who received manual therapy was similar within each treatment group (ie, ST responders: 86%; ST nonresponders: 88%; NM responders: 50%; NM nonresponders: 56%). It is unlikely that manual therapy is required as an adjunct to exercise-based interventions aimed at improving CLBP-related disability. Placebo effects are likely responsible for some of the symptomatic benefits observed in both groups, as there is a placebo effect associated with exercise.[12]

TABLE 4 Difference in Mean Change (Baseline Minus Follow-up) Between Groups Over Time (NM Group Minus ST Group) for All Outcomes

	Baseline to 6 weeks		Baseline to 12 weeks	
	Difference in Mean Change From Baseline Between Groups (NM Group - ST Group) (95% CI)	*P* Value	Difference in Mean Change From Baseline Between Groups (NM group - ST Group) (95% CI)	*P* Value
Primary Outcome				
Oswestry Disability Index (ODI %)	−2.25 (−7.19, 2.69)	0.37	−4.39 (−10.19, 1.41)	0.14
Secondary Outcomes				
Pain intensity (NRS)	−0.09 (−1.18, 1.00)	0.87	0.10 (−1.15, 1.36)	0.87
Tampa Scale for Kinesiophobia (TSK-17)	−0.38 (−4.06, 3.30)	0.84	−1.33 (−5.46, 2.81)	0.53
Pain Self-Efficacy Questionnaire (PSEQ)	0.56 (−3.35, 4.47)	0.78	1.80 (−2.50, 6.09)	0.41
International Physical Activity Questionnaire - Short Form (IPAQ-SF) (METs)	1758 (−434, 3951)	0.12	−559 (−2750, 1631)	0.62
Additional Outcomes				
Lumbar extension strength (N·m)	−2.86 (−39.90, 34.18)	0.88	5.37 (−38.06, 48.80)	0.81
Force matching error	2.99 (1.52, 4.46)	<0.01	0.54 (−0.95, 2.04)	0.48
Average lifting time (s)	0.47 (−0.04, 0.98)	0.07	0.27 (−0.23, 0.77)	0.29
Max knee ROM during lifting (°)	6.10 (−6.33, 18.53)	0.34	8.42 (−5.30, 22.14)	0.23
Max hip ROM during lifting (°)	2.24 (−3.67, 8.14)	0.46	−2.19 (−8.18, 3.80)	0.47
Max lumbar ROM during lifting (°)	−0.75 (−5.98, 4.49)	0.78	2.39 (−3.14, 7.91)	0.40
Asymmetric WB mean during lifting (kg)	1.02 (−1.01, 3.06)	0.32	1.99 (−0.29, 4.27)	0.09
Asymmetric WB SD during lifting (kg)	0.20 (−1.51, 1.92)	0.81	−0.55 (−2.49, 1.38)	0.57
LM thickness (cm)	0.00 (−0.19, 0.20)	0.97	−0.04 (−0.26, 0.19)	0.74

Abbreviations: CI, confidence interval; LM, lumbar multifidus; METs, metabolic equivalents; NM, neuromuscular; NRS, Numeric Rating Scale; ROM, range of motion; SD, standard deviation; ST, strengthening; WB, weight-bearing.

Clinical Implications

Albeit not demonstrated statistically, our study is meaningful because it demonstrates that trunk and lower-limb resistance exercises produce clinically important improvements in disability and pain in a highly disabled CLBP cohort. People with disabling CLBP are commonly managed with opioid medication[50] that is ineffective in the long term and can have serious adverse effects.[5] Furthermore, surgical interventions where there is an absence of nerve root compression is also ineffective,[1] costly, and potentially harmful.[3,15,19] Clinical guidelines emphasize nonmedicated and nonsurgical treatment options involving exercise.[37] We found that progressive overload training that complies with the American College of Sports Medicine guidelines[20] is effective at improving symptomatic outcomes, as well as strength and neuromuscular control in people with CLBP. No adverse events were reported by therapists in this study.

Strengths and Limitations

Strengths of this RCT include a low risk of bias. Specifically, the blinding of participants and assessors reduces the risk of overestimation of treatment effects on patient-reported outcomes.[58] while details pertaining to the intervention (ie, specific exercises and dosages) enable accurate reproducibility by researchers and clinicians.

We recruited low overall participant numbers and had missing follow-up data given early cessation of the RCT secondary to government-imposed COVID-19 restrictions. However, we applied multiple imputation to help limit the impact of this early cessation for those participants who provided follow-up data. No subcategorization of participants with CLBP limits the understanding of the treatment effects on subgroups, given it is well understood that people with CLBP are not homogenous.[40,54] We did not include a placebo group. However, neuromuscular control exercise is superior to placebo treatment for people with CLBP.[9]

Future Research

Future studies are required to determine the mechanisms involved with reduced disability from exercise in people with CLBP. Studies should aim to subgroup participants based on clinically identifiable characteristics (eg, disability level, specific to one's functional deficits, movement patterns during functional tasks). Studies with extended follow-up times are needed to evaluate outcomes post cessation of treatment and the likelihood of continued self-management. Future research could also investigate the efficacy of applying the

exercises and dosages used in this study to nonmachine-based programs (eg, free weights and/or resistance bands), allowing the protocol to be more versatile.

CONCLUSION

Patients who completed 12 weeks of resistance training with or without combined neuromuscular control exercises had clinically important reductions in CLBP-related disability, pain intensity, and kinesiophobia. Retraining lumbar extensor neuromuscular control in combination with strengthening exercises yielded no greater improvements in self-reported disability than strengthening exercises alone.

KEY POINTS

FINDINGS: Resistance training with or without neuromuscular control retraining can yield clinically important improvements in meaningful (ie, pain and disability) outcomes for people with chronic low back pain (CLBP). Twelve weeks of resistance exercise resulted in a meaningful change, a psychological outcome (ie, kinesiophobia), but not in neuromuscular or biomechanical outcomes.

IMPLICATIONS: Neuromuscular retraining of lumbar extensor muscles may not be required to create meaningful changes to important outcomes for people with CLBP. People with CLBP may not need to demonstrate physical deficits to benefit from resistance exercises.

CAUTION: Participants were not subcategorized, and it is possible that some individuals with CLBP require neuromuscular retraining to yield clinically important improvements in disability and pain.

STUDY DETAILS

AUTHOR CONTRIBUTIONS: Joshua Farragher: Conceptualization, study design, data collection and analysis, interpretation of results, and drafting the manuscript. Adrian Pranata: Conceptualization, study design, data analysis, results interpretation, and editing the manuscript. Gavin Williams: Conceptualization, study design, results interpretation, and editing the manuscript. Doa El-Ansary: Conceptualization, study design, results interpretation, and editing the manuscript. Selina Parry: Conceptualization, study design, and editing the manuscript. Ross Clark: Data analysis results interpretation and editing the manuscript. Benjamin Mentiplay: Data analysis, results interpretation, and editing the manuscript. Jessica Kasza: Statistical analysis and review of the manuscript. Samuel Crofts: Statistical analysis and review of the manuscript. Adam Bryant: Conceptualization, study design, data analysis, results interpretation, and editing the manuscript. All authors have read and approved the final version of the manuscript.

DATA SHARING: Data are available upon request. Individual participant data that underlie the results reported in this article, after deidentification, will be made available upon request to researchers who provide a methodological sound proposal immediately following publication. Requests for data should be made to the corresponding author Dr Joshua Farragher via e-mail: joshua.farragher@rmit.edu.au.

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REFERENCES

1. Bono CM, Lee CK. Critical analysis of trends in fusion for degenerative disc disease over the past 20 years. *Spine.* 2004;29:455-463. https://doi.org/10.1097/01.BRS.0000090825.94611.28
2. Booth M. Assessment of physical activity: an international perspective. *Res Q Exerc Sport.* 2000;71:114-120. https://doi.org/10.1080/02701367.2000.11082794
3. Brox JI, Sorensen R, Friis A, et al. Randomized clinical trial of lumbar instrumented fusion and cognitive intervention and exercises in patients with chronic low back pain and disc degeneration. *Spine.* 2003;28:1913-1921. https://doi.org/10.1097/01.BRS.0000083234.62751.7A
4. Carpenter JR, Kenward MG. *Multiple Imputation and Its Application*. Chichester, UK: Wiley; 2013
5. Chaparro LE, Furlan AD, Deshpande A, Mailis-Gagnon A, Atlas S, Turk DC. Opioids compared to placebo or other treatments for chronic low-back pain. *Cochrane Database Syst Rev.* 2013;CD004959. https://doi.org/10.1002/14651858.CD004959.pub4
6. Chiarotto A, Deyo RA, Terwee CB, et al. Core outcome domains for clinical trials in non-specific low back pain. *Eur Spine J.* 2015;24:1127-1142. https://doi.org/10.1007/s00586-015-3892-3
7. Chiarotto A, Maxwell LJ, Ostelo RW, Boers M, Tugwell P, Terwee CB. Measurement properties of visual analogue scale, numeric rating scale, and pain severity subscale of the brief pain inventory in patients with low back pain: a systematic review. *J Pain.* 2019;20:245-263. https://doi.org/10.1016/j.jpain.2018.07.009
8. Chiarotto A, Vanti C, Cedraschi C, et al. Responsiveness and minimal important change of the pain self-efficacy questionnaire and short forms in patients with chronic low back pain. *J Pain.* 2016;17:707-718. https://doi.org/10.1016/j.jpain.2016.02.012
9. Costa LO, Maher CG, Latimer J, et al. Motor control exercise for chronic low back pain: a randomized placebo-controlled trial. *Phys Ther.* 2009;89:1275-1286. https://doi.org/10.2522/ptj.20090218
10. Craig CL, Marshall AL, Sjostrom M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc.* 2003;35:1381-1395. https://doi.org/10.1249/01.MSS.0000078924.61453.FB
11. Cro S, Morris TP, Kahan BC, Cornelius VR, Carpenter JR. A four-step strategy for handling missing outcome data in randomised trials affected by a pandemic. *BMC Med Res Methodol.* 2020;20:208. https://doi.org/10.1186/s12874-020-01089-6
12. Crum AJ, Langer EJ. Mind-set matters: exercise and the placebo effect. *Psychol Sci.* 2007;18:165-171. https://doi.org/10.1111/j.1467-9280.2007.01867.x
13. Dailey DL, Keffala VJ, Sluka KA. Do cognitive and physical fatigue tasks enhance pain, cognitive fatigue, and physical fatigue in people with fibromyalgia? *Arthritis Care Res (Hoboken).* 2015;67:288-296. https://doi.org/10.1002/acr.22417
14. Davidson M, Keating JL. A comparison of five low back disability questionnaires: reliability and responsiveness. *Phys Ther.* 2002;82:8-24. https://doi.org/10.1093/ptj/82.1.8

15. Deyo RA, Mirza SK, Martin BI, Kreuter W, Goodman DC, Jarvik JG. Trends, major medical complications, and charges associated with surgery for lumbar spinal stenosis in older adults. *JAMA.* 2010;303:1259-1265. https://doi.org/10.1001/jama.2010.338
16. Fairbank JC, Couper J, Davies JB, O'Brien JP. The Oswestry low back pain disability questionnaire. *Physiotherapy.* 1980;66:271-273. https://doi.org/10.1037/t04205-000
17. Farragher JB, Pranata A, Williams G, et al. Effects of lumbar extensor muscle strengthening and neuromuscular control retraining on disability in patients with chronic low back pain: a protocol for a randomised controlled trial. *BMJ Open.* 2019;9:e028259. https://doi.org/10.1136/bmjopen-2018-028259
18. Ferrari S, Vanti C, Pellizzer M, Dozza L, Monticone M, Pillastrini P. Is there a relationship between self-efficacy, disability, pain and sociodemographic characteristics in chronic low back pain? A multicenter retrospective analysis. *Arch Physiother.* 2019;9:9. https://doi.org/10.1186/s40945-019-0061-8
19. Fritzell P, Hagg O, Wessberg P, Nordawall A. 2001 Volvo Award Winner in Clinical Studies: lumbar fusion versus nonsurgical treatment for chronic low back pain. *Spine.* 2001;26:2521-2534. https://doi.org/10.1097/00007632-200112010-00002
20. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc.* 2011;43:1334-1359. https://doi.org/10.1249/MSS.0b013e318213fefb
21. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet (London, England).* 2020;396:1204-1222. https://doi.org/10.1016/S0140-6736(20)30925-9
22. Goubert L, Crombez G, Van Damme S, Vlaeyen JW, Bijttebier P, Roelofs J. Confirmatory factor analysis of the Tampa Scale for Kinesiophobia: invariant two-factor model across low back pain patients and fibromyalgia patients. *Clin J Pain.* 2004;20:103-110. https://doi.org/10.1097/00002508-200403000-00007
23. Grotle M, Vollestad NK, Veierod MB, Brox JI. Fear-avoidance beliefs and distress in relation to disability in acute and chronic low back pain. *Pain.* 2004;112:343-352. https://doi.org/10.1016/j.pain.2004.09.020
24. Hartvigsen J, Hancock MJ, Kongsted A, et al. What low back pain is and why we need to pay attention. *The Lancet.* 2018;391:2356-2367. https://doi.org/10.1016/S0140-6736(18)30480-X
25. Hayden JA, Van Tulder MW, Malmivaara A, Koes BW. Exercise therapy for treatment of non-specific low back pain. *Cochrane Database Syst Rev.* 2005;3:CD000335. https://doi.org/10.1002/14651858.CD000335.pub2
26. Hodges PW, Richardson CA. Inefficient muscular stabilization of the lumbar spine associated with low back pain. A motor control evaluation of transversus abdominis. *Spine (Phila Pa 1976).* 1996;21:2640-2650. https://doi.org/10.1097/00007632-199611150-00014
27. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ.* 2014;348:g1687. https://doi.org/10.1136/bmj.g1687
28. Huijnen IP, Verbunt JA, Peters ML, et al. Do depression and pain intensity interfere with physical activity in daily life in patients with Chronic Low Back Pain? *Pain.* 2010;150:161-166. https://doi.org/10.1016/j.pain.2010.04.021
29. James KE, Bloch DA, Lee KK, Kraemer HC, Fuller R. An index for assessing blindness in a multi-centre clinical trialL disulfiram for alcohol cessation-a VA cooperative study. *Stat Med.* 1996;15:1421-1434. https://doi.org/10.1002/(SICI)1097-0258(19960715)15:13<1421::AID-SIM266>3.0.CO;2-H
30. Jamison RN, Raymond SA, Slawsby EA, McHugo GJ, Baird JC. Pain assessment in patients with low back pain: comparison of weekly recall and momentary electronic data. *J Pain.* 2006;7:192-199. https://doi.org/10.1016/j.jpain.2005.10.006
31. Lima LV, Abner TSS, Sluka KA. Does exercise increase or decrease pain? Central mechanisms underlying these two phenomena. *J Physiol.* 2017;595:4141-4150. https://doi.org/10.1113/JP273355
32. Mannion AF, Junge A, Taimela S, Muntener M, Lorenzo K, Dvorak J. Active therapy for chronic low back pain part 3. Factors influencing self-rated disability and its change following therapy. *Spine.* 2001;26:920-929. https://doi.org/10.1097/00007632-200104150-00015
33. Maughan EF, Lewis JS. Outcome measures in chronic low back pain. *Eur Spine J.* 2010;19:1484-1494. https://doi.org/10.1007/s00586-010-1353-6
34. Miller RP, Kori SH, Todd DD. The Tampa Scale: a measure of kinisophobia. *Clin J Pain.* 1991;7:51. https://doi.org/10.1097/00002508-199103000-00053
35. Monticone M, Ambrosini E, Rocca B, Foti C, Ferrante S. Responsiveness and minimal clinically important changes for the Tampa Scale of Kinesiophobia after lumbar fusion during cognitive behavioral rehabilitation. *Eur J Phys Rehabil Med.* 2017;53:351-358. https://doi.org/10.23736/S1973-9087.16.04362-8
36. Nicholas MK. The pain self-efficacy questionnaire: taking pain into account. *Eur J Pain.* 2007;11:153-163. https://doi.org/10.1016/j.ejpain.2005.12.008
37. Oliveira CB, Maher CG, Pinto RZ, et al. Clinical practice guidelines for the management of non-specific low back pain in primary care: an updated overview. *Eur Spine J.* 2018;27:2791-2803. https://doi.org/10.1007/s00586-018-5673-2
38. Oliveira DS, Velia Ferreira Mendonca L, Sofia Monteiro Sampaio R, Manuel Pereira Dias de Castro-Lopes J, Ribeiro de Azevedo LF. The impact of anxiety and depression on the outcomes of chronic low back pain multidisciplinary pain management—a multicenter prospective cohort study in pain clinics with one-year follow-up. *Pain Med.* 2019;20:736-746. https://doi.org/10.1093/pm/pny128
39. Ostelo RWJG, Deyo RA, Stratford P, et al. Interpreting change scores for pain and functional status in low back pain- towards international consensus regarding minimal important change. *Spine.* 2008;33:90-94. https://doi.org/10.1097/BRS.0b013e31815e3a10
40. O'Sullivan P. It's time for change with the management of non-specific chronic low back pain. *Br J Sports Med.* 2012;46:224-227. https://doi.org/10.1136/bjsm.2010.081638
41. Pengel LH, Refshauge KM, Maher CG. Responsiveness of pain, disability, and physical impairment outcomes in patients with low back pain. *Spine (Phila Pa 1976).* 2004;29:879-883. https://doi.org/10.1097/00007632-200404150-00011
42. Polaski AM, Phelps AL, Kostek MC, Szucs KA, Kolber BJ. Exercise-induced hypoalgesia: a meta-analysis of exercise dosing for the treatment of chronic pain. *PLOS ONE.* 2019;14:e0210418. https://doi.org/10.1371/journal.pone.0210418
43. Pranata A, Perraton L, El-Ansary D, et al. Lumbar extensor muscle force control is associated with disability in people with chronic low back pain. *Clin Biomech (Bristol, Avon).* 2017;46:46-51. https://doi.org/10.1016/j.clinbiomech.2017.05.004
44. Pranata A, Perraton L, El-Ansary D, et al. Trunk and lower limb coordination during lifting in people with and without chronic low back pain. *J Biomech.* 2018;71:257-263. https://doi.org/10.1016/j.jbiomech.2018.02.016
45. Roelofs J, Goubert L, Peters ML, Vlaeyen JW, Crombez G. The Tampa Scale for Kinesiophobia: further examination of psychometric properties in patients with chronic low back pain and fibromyalgia. *Eur J Pain.* 2004;8:495-502. https://doi.org/10.1016/j.ejpain.2003.11.016
46. Sanchez-Zuriaga D, Lopez-Pascual J, Garrido-Jaen D, de Moya MF, Prat-Pastor J. Reliability and validity of a new objective tool for low back pain functional assessment. *Spine (Phila Pa 1976).* 2011;36:1279-1288. https://doi.org/10.1097/BRS.0b013e3181f471d8
47. Saragiotto BT, Maher CG, Yamato TP, et al. Motor control exercise for chronic non-specific low-back pain. *Cochrane Database Syst Rev.* 2016;CD012004. https://doi.org/10.1002/14651858.CD012004
48. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *Ann Intern Med.* 2010;152:1-7. https://doi.org/10.7326/0003-4819-152-11-201006010-00232

49. Searle A, Spink M, Ho A, Chuter V. Exercise interventions for the treatment of chronic low back pain: a systematic review and meta-analysis of randomised controlled trials. *Clin Rehabil.* 2015;29:1155-1167. https://doi.org/10.1177/0269215515570379

50. Shmagel A, Ngo L, Ensrud K, Foley R. Prescription medication use among community-based U.S. adults with chronic low back pain: a cross-sectional population based study. *J Pain.* 2018;19:1104-1112. https://doi.org/10.1016/j.jpain.2018.04.004

51. Sluka KA, Frey-Law L, Hoeger Bement M. Exercise-induced pain and analgesia? Underlying mechanisms and clinical translation. *Pain.* 2018;159:S91-S97. https://doi.org/10.1097/j.pain.0000000000001235

52. Suzuki H, Aono S, Inoue S, et al. Clinically significant changes in pain along the Pain Intensity Numerical Rating Scale in patients with chronic low back pain. *PLOS ONE.* 2020;15:e0229228. https://doi.org/10.1371/journal.pone.0229228

53. Tsutsumi T, Don BM, Ziachkowsky LD, Delizonna LL. Physical fitness and psychological benefits of strength training in community dwelling older adults. *J Physiol Antrhopology.* 1997;16:257-266. https://doi.org/10.2114/jpa.16.257

54. Wand BM, O'Connell NE. Chronic non-specific low back pain - sub-groups or a single mechanism? *BMC Musculoskelet Disord.* 2008;9:11. https://doi.org/10.1186/1471-2474-9-11

55. Warburton DE, Nicol CW, Bredin SS. Health benefits of physical activity: the evidence. *CMAJ.* 2006;174:801-809. https://doi.org/10.1503/cmaj.051351

56. Wewege MA, Booth J, Parmenter BJ. Aerobic vs. resistance exercise for chronic non-specific low back pain: a systematic review and meta-analysis. *J Back Musculoskelet Rehabil.* 2018;31:889-899. https://doi.org/10.3233/BMR-170920

57. White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med.* 2011;30:377-399. https://doi.org/10.1002/sim.4067

58. Wood L, Egger M, Gluud LL, et al. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *BMJ.* 2008;336:601-605. https://doi.org/10.1136/bmj.39465.451748.AD