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Tailored versus standardized rehabilitation for patients with shoulder pain: a feasibility randomized controlled trial (the Otago MASTER trial)

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Abstract

Objectives

The aim of this study was to assess whether it was feasible to conduct a full trial comparing a tailored versus a standardized rehabilitation for patients with shoulder pain.

Design

Two-arm, patient- and assessor-blinded, randomized controlled feasibility trial.

Methods

Participants with subacromial disorders of the shoulder were randomly allocated into one of two intervention groups – tailored or standardized rehabilitation. The primary outcome measures were (1) the participant recruitment rate; (2) the proportion of participants enrolled from the total number screened; (3) drop-out rates; and (4) adherence to the rehabilitation programme. The secondary outcome measures were: (5) pain levels; (6) patient specific functional scale (PSFS); (7) the Shoulder Pain and Disability Index (SPADI); and (8) pain self-efficacy. We compared changes in pain and disability scores between groups using a repeated mixed-model analysis of variance. Since this is a feasibility study, we did not adjust alpha for multiple comparisons, and considered 75% CI as the probability threshold at 3-month follow-up. Health-related quality of life was assessed using the Short-Form 12 and quality-adjusted life years (QALYs) were estimated.

Results

Twenty-eight participants were randomly allocated to a tailored rehabilitation programme (n=13) or a standardized rehabilitation programme (n=15). The recruitment rate was 3 participants per month, the proportion of participants enrolled was 23%, the drop-out rate was 14%, and the overall adherence to the rehabilitation programme was 85%. No between-group differences were found for most secondary outcome measures. Adverse events (n=22; 9 in standardised group, 13 in tailored group) were minor in nature and included delayed onset muscle soreness, skin injury or pain following taping.

Conclusions

Our feasibility trial showed that additional strategies are required for improving recruitment, enrolment and minimizing drop-out of participants into the trial and making it feasible to conduct a full trial.

Ethics

This study was approved by the University of Otago Ethics Committee [H17/080].

Trial registration number

ANZCTR: 12617001405303.

Keywords

Shoulder, rehabilitation, manual therapy, feasibility trial.

Word count

3880

Strengths and limitations of this study

- Our findings suggest it is feasible to conduct the full trial. Most participants adhered to the rehabilitation programme, and the drop-out rate was within *a priori* bounds.
- The protocols used for both intervention arms had detailed information about how to progress with exercises over the intervention period.
- Clinicians received training sessions to familiarize themselves with the protocol and the trial only started after clinicians received the training and considered themselves familiarized with interventions from both arms.
- Session duration is not representative of current practice in New Zealand, however, current practices should not refrain research from testing new interventions that may deliver better care for patients with shoulder disorders.

Tailored versus standardized rehabilitation for patients with shoulder pain: a feasibility randomized controlled trial (the Otago MASTER trial)

Introduction

Shoulder pain is the third most common musculoskeletal complaint, with a one-year prevalence of 18.1%.[1] This high prevalence in combination with the significant disability caused by shoulder pain results in high burden – the average annual cost of shoulder subacromial pain has been estimated at $4,139 per patient, in Sweden,[2] and in NZ costs for shoulder injuries totalled NZ$14 million/year in on average from 2005 to 2013.[3]

Shoulder subacromial pain is defined as pain at the top and lateral part of the shoulder joint, may spread to the neck and elbow, and is worsened by overhead activity.[4] It has a slow recovery,[5] with only 50% of new episodes presenting full recovery within 6 months.[6] Best evidence recommends exercise therapy be prescribed for patients with shoulder subacromial pain;[7] however, the strength of evidence supporting this recommendation is limited as most previous trials have had small sample size, short-term follow-up and high risk of bias.[8 9] One large trial, with low risk of bias, compared exercise therapy to placebo and reported no differences between groups.[10] A Cochrane Review recommended additional trials to compare exercise therapy to placebo,[9] while two recent reviews suggested future trials to compare different types, dose or duration of exercise therapy regimens.[8 11] Future trials should include a control arm (e.g. usual care) to establish efficacy as well as compare different forms of exercise interventions.

The role of manual therapy in the management of patients with shoulder subacromial pain is also unclear. A recent systematic review suggests that manual therapy may be beneficial for patients with shoulder subacromial pain at early stages of rehabilitation.[8] Preliminary evidence indicates that sustained shoulder mobilization may reduce pain and improve range of motion in patients with shoulder subacromial pain, compared to sham sustained mobilization.[12] Evidence from trials on other musculoskeletal disorders suggest that including manual therapy led to better clinical outcomes when compared to corticosteroid injection or wait-and-see in the management of other musculoskeletal disorders (e.g. tennis elbow),[13] or usual care when managing patients with hip or knee osteoarthritis.[14]

The aim of our full study is to assess the clinical- and cost-efficacy of a tailored rehabilitation programme versus a standardised rehabilitation programme versus usual care for the treatment of shoulder subacromial pain. Prior to conducting a fully-powered randomized controlled trial (RCT), we conducted a feasibility trial to assess: (1) the participant recruitment rate; (2) the proportion of participants enrolled from the total number screened; (3) adherence to the rehabilitation programme; (4) drop-out rates; (5) preliminary estimates of adverse events; (6) preliminary estimates of intervention effects in order to inform the sample size of the fully-powered RCT; and (7) the feasibility of collecting costs-related data within the trial.

Methods

Trial design

The Management of subacromial disorders of the shoulder (MASTER) trial is a two-arm, patient- and assessor-blinded, feasibility randomized controlled trial. Participants were randomly allocated into one of two intervention groups: a standardized or a tailored rehabilitation programme.

We followed the Consolidated Standards of Reporting Trials (CONSORT) statement for non-pharmacological treatment.[15] In addition, we followed the Template for Intervention Description and Replication (TIDieR) checklist and guide.[16] The study protocol was prospectively registered with the Australian and New Zealand Clinical Trials Registry (ANZCTR: 12617001405303) and published.[17] This study was approved by the University of Otago Ethics Committee [H17/080].

Participants

We recruited participants with shoulder subacromial pain, aged from 18 to 65 years old, from within the Dunedin area (New Zealand) through newspaper advertisements. Participants were screened by a musculoskeletal physiotherapist, following the British Elbow and Shoulder Society (BESS) guidelines.[4] Given the challenges in diagnosing patients with shoulder pain and the low sensitivity of most clinical tests for the shoulder disorders,[18] we widened the criteria proposed by BESS and added resisted lateral rotation and shoulder abduction.[19] The resisted external rotation test has 100% specificity and 34% sensitivity for identifying any degree of subacromial disorder with accuracy of 42%,.[19] Resisted shoulder abduction has 55% sensitivity, 75% specificity, 57% accuracy and a likelihood ratio of 2.2 for identifying any degree of subacromial disorder. Pain on external rotation is the most accurate test reported for identifying partial-thickness tear.

The BESS guidelines screen for red flags (e.g. tumour, unreduced dislocation, acute rotator cuff tear, infection), shoulder pain with cervical spine origin, shoulder instability, acromioclavicular joint disease, or adhesive capsulitis.[4] Participants were included if they presented a positive finding on one of the following tests: (1) Painful arc movement during shoulder flexion or abduction; (2) Jobe's test;[4] or (3) pain on resisted lateral rotation or abduction.[19]

We excluded participants with a history of shoulder dislocation, shoulder subluxation, shoulder surgery and cervical surgery within the last 6 months,[20] participants with any kind of symptoms of systematic inflammation or disease, signs of paraesthesia in the upper extremities, hemiplegic shoulder pain, frozen shoulder, or positive clinical signs of full thickness rotator cuff tear.[21]

All participants provided written consent prior to taking part in the study.

Interventions

Participants in both groups received 16 individual, face-to-face sessions, each lasting for approximately 60 min, over an 8-week period. The tailored and standardized rehabilitation interventions are described on the Supplementary Material S1 and S2 respectively.

Participants performed 8 exercises per session, plus three stretches (control group) or up to three manual therapy techniques (tailored group). To enhance internal validity of the trial, the dosage of exercises for each group was planned to be equivalent. The intensity of strengthening exercises was monitored using a modified Borg scale.[22]

Tailored rehabilitation: participants allocated to the tailored rehabilitation group received exercises focusing on restoring normal movement pattern and the dynamic stability of the scapulothoracic and glenohumeral joints,[23 24] in addition to manual therapy techniques for restoring shoulder and scapular movement[25] and motor control and reducing pain, and progressive resistance training of impaired muscles.[24 26]

Standardized rehabilitation: participants allocated to this group received progressive resistance training for all scapular and shoulder muscles and a stretching exercise programme.[27] This intervention focused on restoring muscle flexibility and strength.

Primary outcome measures

The primary outcome measures were: (1) the participant recruitment rate, measured as number of participants enrolled per month; (2) the proportion of participants enrolled from the total number screened, with reasons for exclusion; (3) drop-out rates, expressed as a percentage of the total number of participants enrolled; and (4) adherence to the rehabilitation programme, measured as number of sessions attended as a percentage of the total number of planned sessions.

Secondary outcome measures

When defining the secondary outcome measures for this feasibility trial, we considered the patient-reported outcome measures intended as the primary and secondary outcomes to be used in the main trial. Hence, the secondary outcome measures were:

(1) Pain intensity (at rest, during movement and average pain during the last 7 days) as measured by a numeric pain scale.[28] The numeric pain scale is a reliable and responsive tool when used with patients with shoulder pain.[29] The minimal clinically important difference (MCID) for the 10-point numeric pain scale in patients with shoulder pain is 1.1 points.[29]

(2) The Patient Specific Functional Scale (PSFS). The PSFS measures disability and is a valid, reliable and responsive tool for assessing patients with shoulder pain.[30] The MCID for the PSFS is 1.3 (for small changes), 2.3 (medium changes) and 2.7 (large changes) in patients with a range of musculoskeletal disorders.[31]

(3) The Shoulder Pain and Disability Index (SPADI) total score (including the pain and disability subscales).[32] The SPADI presents acceptable construct validity and responsiveness in patients with shoulder pain.[33] According to a systematic review, the MCID for the SPADI total score ranges from 8 to 13.[34]

(4) The pain self-efficacy questionnaire.[35] The pain self-efficacy questionnaire is an established and commonly used tool for assessing self-efficacy in individuals with pain.[36] The MCID for the pain self-efficacy questionnaire is 9 points for patients with low back pain.[37]

We assessed safety by recording all adverse events, both related and unrelated to interventions, in each group. The literature suggests adverse events to exercise therapy might be common, but not serious.[38] Potential adverse reactions to interventions may include muscle soreness or increased pain around the shoulder joint. The physiotherapist recorded any adverse reactions to interventions, including duration and severity of adverse reaction to treatment, and how the adverse reaction was managed. We included in the report the total number of participants who reported adverse events, relatedness to interventions, and the duration and severity of the adverse reactions. In the small sample of this feasibility trial, we did not expect to observe a representative number of adverse events, so did not undertake statistical comparisons.

Economic outcomes

Health-related quality of life was assessed using the Short-Form 12 (SF-12v2) questionnaire.[39] To allow the calculation of health utility values for the economic evaluation the SF-12v2 was converted to a six-dimensional health state classification (SF-6D).[40] Health utility is a preference-based measure of overall health-related quality of life, on a scale from 0 (equivalent to death) to 1 (full health). Quality-adjusted life years (QALYs) were estimated for each participant by calculating the area under the curve (the product of utility values by time) from baseline to 12-week follow-up. We calculated the mean QALYs for each group and adjusted for baseline utility scores to minimize any bias due to chance of baseline imbalance between the groups.

We adapted the Otago Cost and Consequences Questionnaire (OCC-Q) to shoulder disorders and used the adapted questionnaire to capture healthcare use and other non-healthcare costs (e.g., time off work).[41] The OCC-Q is a validated patient-administered questionnaire developed for osteoarthritis that has demonstrated accuracy and agreement with administrative databases in the New Zealand healthcare system.[41] The OCC-Q was administered at baseline and 12-week time points. Costs are expressed as 2019 NZ dollars, exclusive of Goods and Services Tax.

Sample size

Given this is a feasibility trial, we did not design it to assess the efficacy of the experimental intervention.[42] [43] Whitehead et al.[44] recommend the sample size of a feasibility study should be estimated based on the expected range for the effect size, the power and alpha (both established *a priori*), and the total number of arms of treatment planned for the full trial.[44]

Whitehead et al.[44] estimated the sample size based on standardized differences of different magnitudes (i.e. extra small, small, medium and large). To estimate sample size, we used the Shoulder Pain and Disability Index (SPADI) as the presumed primary outcome measure for the full trial and assumed a minimum clinically important difference of 8 points,[45] with a standard deviation of 24 points.[45] This represents a standardized effect size of 0.3. We considered a full trial with power of 80%, two-tailed between-group comparison, and alpha at 0.05. Therefore, the minimum sample size for this feasibility RCT is 10 participants per arm of treatment, assuming a medium effect size.[44] Assuming a 20% loss to follow-up,[46] we aimed for a minimum sample size of 25 participants.

Randomization

Sequence generation, allocation concealment, implementation

Participants were allocated (1:1 ratio) into one of the intervention groups (i.e., tailored physiotherapy or standardized physiotherapy) through blocked randomization (with blocks of 4). The randomisation schedule was computer-generated by a research administrator not involved with delivering the interventions, and concealed in numbered, sealed, and opaque envelopes. A research administrator provided the envelope to the clinician delivering the interventions.

Blinding

Participants and outcome assessors were blinded to group allocation. Clinicians delivering the interventions were not blinded to group allocations due to nature of interventions.

Time points

Outcome measures were recorded at baseline and at the 4th, 8th, and 12th weeks after baseline.

Statistical analysis

We used descriptive statistics analyses for presenting: (1) recruitment rates; (2) proportion of participants enrolled from the total number screened; (3) drop-out rates; (4) adherence to the rehabilitation programme; and (5) adverse events and for reporting economic outcomes. The primary and secondary analyses were intention-to-treat and involved all patients who were randomly assigned. All statistical analysis were conducted using R.[47]

We used linear mixed-effect models to obtain estimates of treatment effects. We conducted within- and between-group comparisons using an independent linear mixed-effect model for each outcome measure (i.e., numeric pain rating scale, PSFS, SPADI pain score, SPADI disability score, SPADI total score, and Pain Self-efficacy). This feasibility trial was not powered to detect superiority; however, we assessed the magnitude of mean treatment effects for pain and disability in relation to clinically important changes. This was done for informing the choice of primary outcome measure to be used in the main trial and thus informing the sample size calculation for the main trial.[48] When running linear mixed-effect models, we estimated marginal means and their respective 75% confidence intervals. For that reason, we did not adjust alpha for multiple comparisons. This statistical approach is considered appropriate for feasibility or exploratory studies.[49]

When conducting within-group comparisons, group allocation (tailored and standardized rehabilitation groups) and 'time-point' (baseline, 4th, 8th week and 12th week) were considered as fixed-effects. Participants were considered as random effects. Post-hoc analyses were conducted for comparing changes in scores between "baseline vs 4 weeks", "baseline vs 8 weeks", and "baseline vs 12 weeks".

When conducting between-group comparisons, group allocation (tailored and standardized rehabilitation groups) and 'time-point' (4th, 8th week and 12th week) were considered as fixed-effects. Participants were considered as random effects. Baseline measurements were considered as covariates. Post-hoc analysis were conducted for comparing scores between groups at each time point (i.e., 4, 8 and 12 weeks).

To help inform whether it is worthwhile conducting the full trial, it is recommended that preliminary between-group comparisons be performed at the feasibility trial stage.[50 51] For that, confidence interval ranges other than 95% are recommended when assessing between-group differences from feasibility trials (e.g. 75% CI in addition to the mean difference estimate).[50] For the purposes of this study, we considered 75% CI as the probability threshold for between-group analyses.[50] Such information will be considered when assessing whether to conduct the full trial.[50 51]

Missing data

Linear mixed-effect models can handle missing data. For descriptive analysis, in case of missing data, we explored pattern of missingness using the "mi" package in R.[52] After running such analysis, we accepted that data was missing at random and performed multiple imputation by chained equations using the "mice" package.[53]

Additional analysis

When running the mixed-effect models, we found residuals presented small deviations from the normal distribution. In those cases, it is recommended to conduct robust mixed-effect models and report estimates from both models (i.e., standard and robust mixed-effect models).[54] We implemented the robust mixed-effect models using the "rlmer" function from WRS 2 package.[54] The robust models had the same input data as the standard mixed-effect models (described above) and yielded similar estimates of treatment effects to those obtained with standard mixed-effect models. For that reason, we report in the main text the estimate effects obtained through the mixed-effect models and reported the estimate effects obtained through the robust mixed-effect models in the Supplementary material.

Results

Recruitment and flow of participants

The recruitment flow and randomization process are presented in Figure 1. The trial started recruiting on 19th January 2018 and completed recruitment on the 23rd of October 2018. The trial ended after recruiting the minimum number of participants as per sample size calculations.

Figure 1

A total of 117 individuals showed interest in taking part in the study and completed telephone screening; 51 were excluded at that screening stage. The main reasons for exclusion were inability to commit to the study, no response after receiving the information sheet or not meeting the inclusion criteria.

Fifty-three participants were physically screened, with 24 participants excluded following physical screening. Reasons for being excluded included (with some participants meeting more than one exclusion criteria): not presenting positive tests to physical examination of the shoulder (n = 12), symptoms caused by neck disorder (n = 7), history of subluxation (n = 1), frozen shoulder (n = 2), AC joint involvement (n = 4), inflammatory disease (n = 3). Following physical screening, 28 participants were eligible for randomization.

Participants' characteristics

The demographics and clinical characteristics of participants are presented in Table 1.

Table 1. Baseline characteristics of 28 participants. Data reported as mean and standard deviation or as count and percentage.

Variables	All participants (N=28)	Standardized exercise group (N=15)	Tailored training group (N=13)
Age (years)	43.89 (9.6)	43.7 (11.7)	44.1 (6.8)
Women	13 (44%)	5 (41%)	4 (40%)
Weight (kg)	82.4 (13.2)	79.4 (12.6)	86.0 (13.5)
Height (cm)	173.2 (10.0)	171.3 (9.7)	175.7 (10.3)
BMI (kg/m2)	27.3 (4.2)	27.2 (4.5)	27.4 (3.9)
Hand dominant, right side	23 (82%)	11 (73%)	12 (92%)
Affected side, dominant shoulder	17 (60%)	10 (66%)	7 (53%)
Shoulder pain duration (months)	49.0 (76.3)	28.3 (28.4)	66.9 (99.8)
Previous history of shoulder pain	6 (21%)	2 (13%)	4 (31%)
Previous treatment of shoulder	9 (32%)	5 (33%)	4 (31%)
Positive painful arc test	86%	80%	92%
Positive Jobe's test	78%	86%	69%
Positive painful resisted external rotation	28%	26%	30%
Positive painful resisted abduction	30%	40%	16%
Pain at rest	2.0 (1.8)	1.6 (1.6)	2.4 (1.9)
Pain during movement	5.3 (2.0)	5.2 (1.9)	5.5 (2.2)
Pain within the last week	4.2 (2.1)	4.0 (2.3)	4.4 (1.9)
Pain self-efficacy	48.0 (9.6)	50.5 (7.2)	45.1 (11.4)
PSFS	4.6 (1.8)	5.0 (1.7)	4.2 (1.8)
SPADI Total	35.5 (15.1)	33.8 (13.3)	37.5 (17.3)
SPADI Pain	51.4 (15.2)	49.8 (15.8)	53.2 (15.0)
SPADI Disability	25.7 (17.1)	24.0 (13.8)	27.7 (20.7)

Abbreviation: PSFS: Patient Specific Functional Scale; SPADI: Shoulder Pain and Disability Index.

Outcomes and estimation

Primary outcome measures

Findings for primary outcome measures are presented in Table 2. The proportion of participants enrolled from the number of participants screened was 23%. The participant recruitment rate (number of participants recruited per month of active recruitment) was 3. The drop-out was 14% for all participants enrolled in the trial. Four participants allocated to the standardized intervention dropped out. Three of the four participants withdrew before initiating physiotherapy intervention: two participants reported being too busy to commit to the study while one participant withdrew as the waiting time to start receiving interventions was considered too long. One participant dropped out of the study after four sessions of intervention, due to moving to another city. All participants allocated to the tailored rehabilitation group completed the trial. The adherence to the rehabilitation programme was 85% for all participants combined, with 73% for participants allocated to the standardized group and 100% for participants in the tailored group.

Table 2. Descriptive statistics for primary outcome measures.

Outcome	All participants (n=28)	Standardized group (n=15)	Tailored group (n=13)
Proportion of participants enrolled from total screened	23%	--	--
Recruitment rate (recruited per month)	3	--	--
Drop-out rates	14%	26%	0%
Adherence to the rehabilitation programme (percentage of sessions attended)	85%	73%	100%

Secondary outcome measures

The descriptive mean scores for pain, disability and pain self-efficacy are presented in Table 10. The within-group changes are presented in Table 11. The estimated marginal mean for between-group differences and their respective 75% confidence intervals are presented in Table 11. The estimated marginal means obtained with the standard and robust mixed-effect analyses are presented in the Supplementary material.

Table 3. Participants' scores for pain, disability, and function at each time point (mean and standard deviation).

	Standardized (n=15)				**Tailored (n=13)**			
	Baseline	4 weeks	8 weeks	12 weeks	Baseline	4 weeks	8 weeks	12 weeks
Pain at rest	1.67 (1.59)	0.9 (0.9)	0.3 (0.5)	0.7 (0.8)	2.4 (1.9)	1.5 (1.3)	0.4 (0.6)	0.4 (0.5)
Pain during movement	5.2 (1.9)	1.3 (0.9)	1.0 (0.5)	1.3 (1.2)	5.5 (2.2)	2.3 (1.8)	1.5 (1.9)	1.1 (1.1)
Pain last week	4.0 (2.3)	1.9 (0.9)	1.3 (0.7)	1.4 (1.2)	4.4 (1.9)	1.8 (1.3)	1.1 (0.8)	1.0 (0.8)
PSFS	5.0 (1.8)	7.1 (1.9)	7.7 (1.3)	6.5 (2.9)	4.2 (1.8)	7.0 (2.2)	7.8 (2.1)	7.2 (2.8)
SPADI Pain	49.8 (15.8)	12.8 (4.6)	17.5 (11.3)	16.8 (15.7)	53.2 (15.0)	15.8 (9.6)	18.6 (12.8)	18.6 (11.9)
SPADI Disability	24.0 (13.9)	9.4 (7.1)	7.0 (6.1)	7.5 (10.0)	27.7 (20.7)	15.8 (11.8)	5.9 (9.3)	6.5 (11.9)
SPADI Total	33.9 (13.3)	16.1 (6.1)	11.2 (6.9)	11.2 (12.0)	37.5 (17.3)	22.0 (13.2)	10.8 (8.4)	11.2 (11.0)
Pain Self-Efficacy	50.5 (7.20)	55.9 (3.2)	55.0 (4.0)	55.9 (5.8)	45.1 (11.4)	53.5 (7.3)	56.2 (5.2)	57.5 (3.4)

PSFS: Patient Specific Functional Scale.

Table 4. Within-group differences (estimated marginal means and 95% confidence intervals).

	Baseline vs 4 weeks		Baseline vs 8 weeks		Baseline vs 12 weeks	
Outcome	Standardized	Tailored	Standardized	Tailored	Standardized	Tailored
Pain at rest	0.9 (0.1 to 1.6)	1.0 (0.2 to 1.7)	1.3 (0.5 to 2.0)	2.0 (1.3 to 2.7)	1.3 (0.5 to 2.0)	2.0 (1.3 to 2.7)
Pain during movement	3.6 (2.6 to 4.5)#	2.8 (1.9 to 3.8)#	4.2 (3.3 to 5.2)#	4.0 (3.1 to 4.9)#	4.2 (3.1 to 5.0)#	4.4 (3.5 to 5.3)#
Pain last week	2.0 (1.2 to 3.0)#	2.3 (1.4 to 3.2)#	2.5 (1.6 to 3.4)#	3.3 (2.4 to 4.2)#	2.6 (1.6 to 3.7)#	3.4 (2.5 to 4.2)#
PSFS	-2.1 (-3.4 to -0.7)	-2.6 (-4.0 to -1.3)#	-2.7 (-4.1 to -1.4)#	-3.7 (-5.0 to -2.3)#	-2.3 (-3.6 to -0.9)	-3.0 (-4.3 to -1.7)#
SPADI Pain	35.8 (28.2 to 43.5)	35.2 (27.7 to 42.7)	31.7 (24.1 to 39.4)	34.6 (27.3 to 41.9)	35.9 (28.2 to 43.6)	34.6 (27.3 to 41.9)
SPADI Disability	12.4 (6.0 to 18.8)	9.7 (3.5 to 15.9)	17.2 (10.7 to 23.6)	21.7 (15.7 to 27.8)	18.3 (11.9 to 24.8)	21.2 (15.1 to 27.2)
SPADI Total	16.02 (10.2 to 21.8)#	13.1 (7.5 to 18.7)	22.6 (16.9 to 28.4)#	26.7 (21.3 to 32.1)#	25.0 (19.2 to 30.7)#	26.3 (20.9 to 31.8)#
Pain Self-efficacy	-3.6 (-6.8 to 0.4)	-7.0 (-10.1 to -3.9)	-5.2 (-8.4 to -2.0)	-11.1 (-14.1 to -8.0)	-6.2 (-9.4 to -3.0)	-12.4 (-15.5 to -9.4)#

Negative values indicate larger scores at follow-up. #: within-group change greater than the minimal clinically important difference.

Table 5. Estimated marginal means and standard error for each group, and between-group estimated marginal mean differences and their respective 75% confidence intervals.

	4 weeks			8 weeks			12 weeks		
Outcome	**Standardized (n=15)**	**Tailored (n=13)**	**Mean difference**	**Standardized (n=15)**	**Tailored (n=13)**	**Mean difference**	**Standardized (n=15)**	**Tailored (n=13)**	**Mean difference**
Pain at rest	0.8 (0.2)	1.3 (0.2)	-0.5 (-0.9 to -0.2)	0.4 (0.2)	0.3 (0.2)	0.1 (-0.3 to 0.4)	0.8 (0.2)	0.3 (0.2)	0.1 (-0.3 to 0.4)
Pain during movement	1.5 (0.4)	2.6 (0.4)	-1.1 (-1.8 to -0.5)	0.9 (0.4)	1.5 (0.4)	-0.6 (-1.3 to 0.0)	1.2 (0.4)	1.1 (0.4)	0.0 (-0.7 to 0.6)
Pain last week	1.9 (0.3)	2.0 (0.2)	-0.1 (-0.5 to 0.3)	0.4 (0.3)	1.0 (0.2)	0.4 (-0.1 to 0.8)	1.1 (0.3)	0.9 (0.2)	0.2 (-0.2 to 0.6)
PSFS	7.0 (0.6)	7.0 (0.6)	0.1 (-0.9 to 1.1)	7.6 (0.6)	8.0 (0.6)	-0.3 (-1.3 to 0.7)	7.9 (0.5)	7.3 (0.6)	-0.1 (-1.1 to 0.9)
SPADI Pain	14.0 (3.1)	17.6 (2.9)	-3.6 (-8.6 to 1.5)	18.1 (3.1)	18.8 (2.9)	0.0 (-5.0 to 5.0)	13.9 (3.1)	18.8 (2.9)	-4.2 (-9.2 to 0.8)
SPADI Disability	10.6 (2.6)	16.1 (2.4)	-5.5 (-9.7 to -1.3)*	5.8 (2.6)	4.8 (2.4)	1.0 (-3.2 to 5.1)	4.7 (2.6)	5.4 (2.4)	-0.7 (-4.9 to 3.4)
SPADI Total	14.4 (2.4)	22.9 (2.2)	-5.5 (-9.4 to -1.6)*	10.8 (2.4)	9.7 (2.2)	1.0 (-2.8 to 4.9)	8.8 (2.4)	10.1 (2.2)	-1.6 (-5.5 to 2.2)
Pain Self-efficacy	54.3 (1.0)	53.7 (1.0)	0.6 (-1.1 to 2.3)	55.9 (1.0)	57.5 (0.9)	-1.6 (-3.3 to 0.0)	56.9 (1.0)	58.9 (0.9)	-2.0 (-3.7 to -0.3)*

Negative differences indicate larger scores for the tailored group; *denotes differences between groups.

Economic outcomes

The mean QALYs and costs regarding visits to healthcare practitioner, healthcare tests or treatment or pain medications at 12 weeks follow-up are presented in Table 13.

Table 6. Total costs (in 2019 NZ$) and health outcomes at 12-week follow-up.

	Standardized group (n=15)	**Tailored group (n=13)**
Cost outcomes		
Healthcare practitioner		
GP	0	480
Physiotherapist	26,400	31,650
Chiropractor	0	150
Acupuncturist	0	0
Massage Therapist	0	225
Healthcare tests / treatment		
X-rays	0	137
Other	0	40**
Cortisone injection	0	0
Medications		
Paracetamol	5	5
NSAID*	0	0
COX-2 inhibitors	0	0
Travel costs	1431	830
Productivity cost	16	1817
Total health system cost	26,405.00	32,687.10
Total societal cost	27,852.27	35,334.04
Health outcomes		
QALYs (SD)	0.17 (0.02)	0.18 (0.02)

**dressings. SD = standard deviation.

Harms

A total of 22 adverse reactions were reported: 9 by participants allocated to the standardized group and 13 by participants allocated to the tailored group (Table 14). Adverse reactions included delayed onset muscle soreness, skin injury following taping of the shoulder and increase in shoulder pain following taping of the shoulder. Two participants allocated to the standardized group had to skip home-based exercises for two consecutive days because of delayed onset muscle soreness.

Table 7. Adverse reactions reported by participants following treatment.

	Total	Standardized	Tailored
DOMS one-to-one session	12	5	7
DOMS home-based exercises	8	4	4
Taping: skin injury	1	0	1
Taping: increase in shoulder pain	1	0	1
Total	22	9	13

DOMS: delayed onset of muscle soreness.

Discussion

This trial assessed the feasibility of conducting a full trial that will compare two forms of exercise therapy for patients with shoulder subacromial pain (one tailored and one standardized rehabilitation programme). Overall, our findings suggest it is feasible to conduct the full trial. Most participants adhered to the rehabilitation programme, and the drop-out rate was within *a priori* bounds.

We identified limitations that must be addressed when designing the full trial. Our ability to enrol participants into the trial during the 9-month period of recruitment was limited by the number of clinicians involved with the study. That impacted on recruitment rate and that can be addressed in the future trial by having a multi-centre design. For the present study, the clinic responsible for delivering the interventions limited the number of participants that could be treated to a maximum of 10 at any given time. That impacted on flow of participants in the trial and prevented us from continuously enrolling participants. Therefore, we had to recruit participants in three stages. Some participants opted to drop-out after being screened for eligibility and notified that there would be a waiting period for interventions to start. When designing the future trial, we will consider a multi-centre design to ensure the minimum sample size required for the full trial is met.

Our findings helped to identify the primary outcome measures to use in the full trial. According to a recent Delphi study, trials on shoulder disorders should assess the following domains: pain, physical functioning, global assessment of treatment success and health-related quality of life.[55] Based on our findings, pain during arm elevation presented the largest changes from baseline to 12-week follow-up for both groups. Recently, it has been recommended that movement-evoked pain should be used for assessing musculoskeletal pain.[56] Our findings also suggested important within-group changes for PSFS and SPADI scores and either of those outcome measures could be used in the full trial. The advantage of PSFS is that it assesses tasks that are especially relevant for a given participant,[32] while, SPADI suffers the limitation of fixed-item instruments, where some items in the questionnaire may not be relevant to a given participant.[32] Based on that, PSFS should be considered as a primary outcome measure in the full trial. In this feasibility study, we did not assess the "global assessment of treatment success" and the future trial should include an outcome measure assessing that construct. We assessed health-related quality of life using the Short-Form 12 (SF-12v2) questionnaire and that should be included in the full trial. When designing the final trial, we will follow the most current recommendations and future work by the Outcome Measures in Rheumatology (OMERACT) Shoulder Working Group.[55 57]

Our sample presented similar scores for pain and slightly lower scores for disability at baseline compared to a large trial with participants with shoulder subacromial pain.[10] Participants in both groups were exposed to active interventions and presented similar changes in pain and function scores over time. The magnitude of changes in pain scores at 12 weeks were greater than those reported by participants exposed to exercise therapy or placebo intervention reported by that large trial.[10] Feasibility and pilot trials are notorious for their imprecise estimates of treatment, given their small sample sizes.[58] For the full trial, we will include an inactive control arm to be able to estimate the effect of standardized or tailored interventions on clinical outcomes.

The trial design had some notable strengths. The protocols used for both intervention arms had detailed information about how to progress with exercises over the intervention period. Clinicians received training sessions to familiarize themselves with the protocol and the trial only started after clinicians received the training and considered themselves familiarized with interventions from both arms. We adopted clinical outcomes that are recommended for trials recruiting patients with shoulder

disorders.[57] Despite the longer duration of interventions, compared to current practice in New Zealand and other countries, participants adhered to both rehabilitation programmes. The number of participants dropping out was low. In the in the standardized rehabilitation group, there was a larger number of participants (n = 3) dropping out after enrolling than the tailored group. The drop-out occurred before starting interventions.

Limitations

One criticism of our design is the duration of the interventions (i.e., sessions lasting for 40-60 min) which is not representative of current practice in New Zealand. On the other hand, findings from one trial suggested higher dosage of exercise therapy led to better clinical outcomes.[59] In addition, current practices should not refrain research from testing new interventions that may deliver better care for patients with shoulder disorders. While our trial will not compare different exercise therapy dosages, it will add valuable information regarding the effect of different forms of exercise therapy delivered at equivalent dosage. In addition, as per our protocol, our nested process evaluation study was conducted parallel to this feasibility trial and will provide more detailed information regarding the participants' and clinicians' perceptions of the interventions tested in this feasibility trial. The information from the current study and the nested process evaluation will be used for improving the design of the full trial.

Conclusions

Our feasibility trial showed that additional strategies are required for improving recruitment, enrolment and minimizing drop-out of participants into the trial. By adopting additional strategies and addressing some of the limitations identified through this feasibility study, it is likely feasible to conduct a full trial assessing the efficacy of a tailored rehabilitation programme.

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Declarations

Patient and Public Involvement

Patients and or public were not involved. Results of this study will be disseminated to study participants by inviting them to join an open-seminar in which the results of the study will be presented. In addition, we will prepare a short report with the main findings of the study and distribute this by e-mail to participants.

Data collection, storage and sharing

We will store participants' data on a secure local server and will use unique identification number on follow-up questionnaires. To protect participants' privacy, all identifying information will be stored separately, and deleted following the conclusion of the trial. We will not share or report identifying information. The datasets generated during the study will be available from the corresponding author on reasonable request.

Confidentiality

The research team will have access to personal information. We will use group mean data to present findings from the study. This will protect confidentiality before, during, and after the trial.

Adverse event management

The risk of a serious adverse event related to the intervention is minimal. We maintained a Data Monitoring Committee (Centre for Health, Activity and Rehabilitation Research—University of Otago) to assess whether it is necessary to report the adverse event to the trial sponsor, and Ethics Committee.

Protocol amendments

We there were no changes to protocol during the implementation of this feasibility trial.

Competing interests statement

None declared.

Authors' contributions

DCR and ZJT conceived the research question. DCR was responsible for the design of the trial, and is the guarantor. ZJT and GS contributed to the design of interventions. JHA provided guidance on the design the trial and economic analysis. RW provided guidance on economic analysis. DCR led efforts for securing funding, with the contributions from ZJT, GS and JHA. All authors revised and approved the protocol for the study. All authors revised the manuscript for important content and approved the final version.

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The Health Research Council – New Zealand had no role in the design of the trial and will have no role in its execution, data analysis and interpretation, or on the submission of the studies for publication.

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Captions

Figure 1. Flow of participants in the trial.

Table 8. Baseline characteristics of 28 participants. Data reported as mean and standard deviation or as count and percentage.

Table 9. Descriptive statistics for primary outcome measures.

Table 10. Participants' scores for pain, disability, and function at each time point (mean and standard deviation).

Table 11. Within-group differences (estimated marginal means and 95% confidence intervals).

Table 12. Estimated marginal means and standard error for each group, and between-group estimated marginal mean differences and their respective 75% confidence intervals.

Table 13. Total costs (in 2019 NZ$) and health outcomes at 12-week follow-up.

Table 14. Adverse reactions reported by participants following treatment.

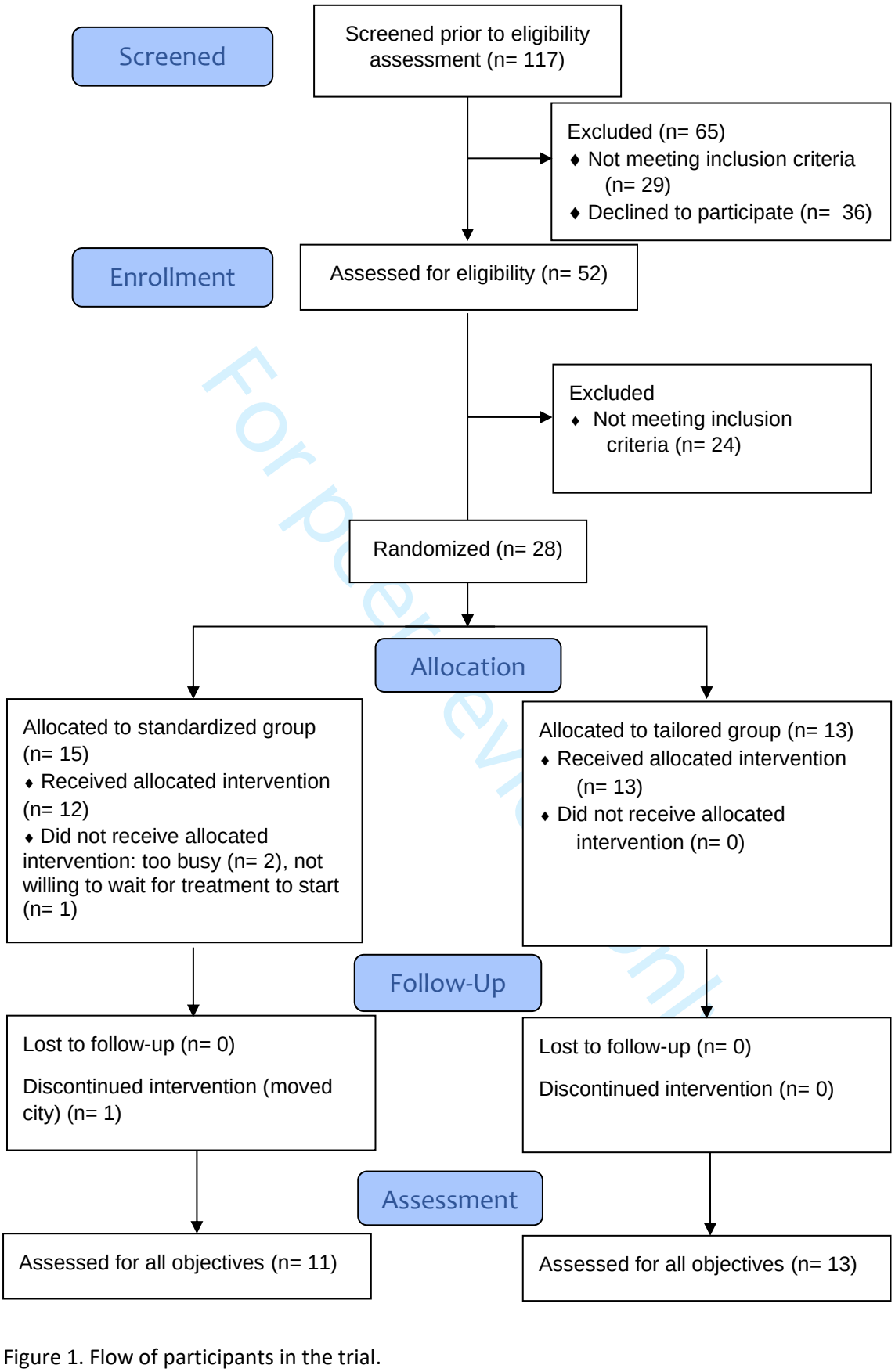

Figure 1. Flow of participants in the trial.

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Supplementary material

The Otago MASTER Trial

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Contents

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1. Overview

Below, we present the estimated marginal means, standard error (SE) and 95% confidence intervals (CI) for estimates when analyzing data using the mixed-effect model, the robust mixed-effect model.

The estimated marginal means and standard errors are very similar between the standard and robust mixed-effect models for all outcomes. For that reason, we presented in the manuscript findings from the standard mixed-effect model in the main manuscript.

2. Pain at rest

2.1. Mixed-effect model

Group	Time point	EMM	SE	95% CI
Standardized	2	0.8	0.2	0.3 to 1.2
Tailored	2	1.3	0.2	0.9 to 1.7
Standardized	3	0.4	0.2	0.0 to 0.8
Tailored	3	0.3	0.2	-0.1 to 0.7
Standardized	4	0.4	0.2	0.0 to 0.8
Tailored	4	0.3	0.2	0.0 to 0.7

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

2.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	0.8	0.2	0.3 to 1.2
Tailored	2	1.2	0.2	0.8 to 1.6
Standardized	3	0.4	0.2	0.0 to 0.8
Tailored	3	0.3	0.2	-0.1 to 0.7
Standardized	4	0.4	0.2	0.0 to 0.8
Tailored	4	0.3	0.2	-0.1 to 0.7

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

3. Pain during movement

3.1. Mixed-effect model

Group	Time point	EMM	SE	95% CI
Standardized	2	1.5	0.4	0.7 to 2.3
Tailored	2	2.6	0.4	1.9 to 3.4
Standardized	3	0.9	0.4	0.1 to 1.7
Tailored	3	1.5	0.4	0.7 to 2.2
Standardized	4	1.0	0.4	0.2 to 1.9
Tailored	4	1.1	0.4	0.3 to 1.9

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

3.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	1.5	0.3	0.8 to 2.1
Tailored	2	2.5	0.3	2.0 to 3.1
Standardized	3	0.8	0.3	0.2 to 1.4
Tailored	3	1.2	0.3	0.6 to 1.7
Standardized	4	1.0	0.3	0.4 to 1.6
Tailored	4	0.9	0.3	0.4 to 1.5

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

4. Pain last week

4.1. Mixed-effect model

Group	Time point	EMM	SE	95% CI
Standardized	2	1.9	0.3	1.3 to 2.4
Tailored	2	2.0	0.2	1.5 to 2.5
Standardized	3	1.4	0.3	0.8 to 1.9
Tailored	3	1.0	0.2	0.5 to 1.5
Standardized	4	1.1	0.3	0.6 to 1.6
Tailored	4	0.9	0.2	0.4 to 1.4

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

4.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	1.8	0.2	1.3 to 2.3
Tailored	2	1.8	0.2	1.4 to 2.3
Standardized	3	1.4	0.2	0.9 to 1.9
Tailored	3	1.0	0.2	0.6 to 1.5
Standardized	4	1.1	0.2	0.6 to 1.6
Tailored	4	0.9	0.2	0.4 to 1.3

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

5. SPADI Pain

5.1. Mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	14.0	3.1	7.8 to 20.3
Tailored	2	17.6	2.9	11.7 to 23.5
Standardized	3	18.1	3.1	11.9 to 24.4
Tailored	3	18.8	2.9	12.4 to 23.9
Standardized	4	13.9	3.1	7.7 to 20.2
Tailored	4	18.8	2.9	12.4 to 23.9

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

5.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	14.0	2.7	8.6 to 19.4
Tailored	2	17.6	2.5	12.5 to 22.6
Standardized	3	16.7	2.7	11.3 to 22.0
Tailored	3	17.1	2.5	12.1 to 22.0
Standardized	4	13.9	2.7	8.5 to 19.3
Tailored	4	16.3	2.5	11.3 to 21.3

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

6. SPADI Disability

6.1. Mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	10.6	2.6	5.4 to 15.8
Tailored	2	16.1	2.4	11.3 to 20.9
Standardized	3	5.8	2.6	0.6 to 11.0
Tailored	3	4.8	2.4	0.1 to 9.6
Standardized	4	4.7	2.6	-0.5 to 9.9
Tailored	4	5.4	2.4	0.6 to 10.2

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

6.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	10.3	1.5	7.3 to 13.4
Tailored	2	13.8	1.4	10.9 to 16.7
Standardized	3	5.6	1.5	2.5 to 8.6
Tailored	3	3.2	1.4	0.3 to 6.0
Standardized	4	4.4	1.5	1.4 to 7.5
Tailored	4	3.7	1.4	0.9 to 6.5

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

7. SPADI Total

7.1. Mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	17.4	2.4	12.6 to 22.2
Tailored	2	22.9	2.2	18.4 to 27.4
Standardized	3	10.8	2.4	5.9 to 15.5
Tailored	3	9.7	2.2	5.3 to 14.2
Standardized	4	8.4	2.4	3.6 to 13.2
Tailored	4	10.1	2.2	5.6 to 14.5

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

7.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	17.2	2.0	13.2 to 21.2
Tailored	2	20.6	1.9	16.8 to 24.3
Standardized	3	10.4	2.0	6.3 to 14.4
Tailored	3	8.7	1.9	5.0 to 12.4
Standardized	4	8.3	2.0	4.2 to 12.3
Tailored	4	8.9	1.9	5.9 to 12.6

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

8. Pain Self-Efficacy

8.1. Mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	54.3	1.0	52.2 to 56.3
Tailored	2	53.7	1.0	51.7 to 55.6
Standardized	3	55.9	1.0	53.9 to 57.9
Tailored	3	57.5	0.9	55.6 to 59.4
Standardized	4	56.9	1.0	54.9 to 58.9
Tailored	4	58.9	0.9	57.0 to 60.8

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

8.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	54.5	0.9	52.7 to 56.2
Tailored	2	54.2	0.8	52.6 to 55.9
Standardized	3	56.2	0.9	54.5 to 58.0
Tailored	3	57.8	0.8	56.2 to 59.4
Standardized	4	57.1	0.9	55.3 to 58.8
Tailored	4	58.6	0.8	57.0 to 60.2

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

9. Patient-specific functional scale

9.1. Mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	7.0	0.6	5.7 to 8.2
Tailored	2	6.9	0.6	5.7 to 9.1
Standardized	3	7.6	0.6	6.3 to 8.9
Tailored	3	7.9	0.6	6.7 to 9.1
Standardized	4	7.2	0.6	5.9 to 8.4
Tailored	4	7.3	0.6	6.1 to 8.4

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

9.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	7.1	0.5	6.0 to 8.2
Tailored	2	6.9	0.5	5.9 to 8.0
Standardized	3	7.6	0.6	6.5 to 8.8
Tailored	3	8.1	0.5	7.1 to 9.1
Standardized	4	7.8	0.6	6.7 to 8.9
Tailored	4	7.8	0.5	6.7 to 8.8

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	1, 4
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	4
	2b	Specific objectives or research questions for pilot trial	4
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	5
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	N.A.
Participants	4a	Eligibility criteria for participants	5
	4b	Settings and locations where the data were collected	5
	4c	How participants were identified and consented	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	5, 6
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	6
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	N.A.
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	N.A.
Sample size	7a	Rationale for numbers in the pilot trial	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N.A.
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	7
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	7
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	7

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	7
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	7
	11b	If relevant, description of the similarity of interventions	5, 6
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	8, 9
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	9
	13b	For each group, losses and exclusions after randomisation, together with reasons	10
Recruitment	14a	Dates defining the periods of recruitment and follow-up	9
	14b	Why the pilot trial ended or was stopped	9
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	12
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	13 to 17
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	14to 17
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	17
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	18
	19a	If relevant, other important unintended consequences	N.A.
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	19
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	18 to 19
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	18 to 19
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	18 to 19
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	5
Protocol	24	Where the pilot trial protocol can be accessed, if available	5
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	24 to 25
	26	Ethical approval or approval by research review committee, confirmed with reference number	2

Citation: Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355.
*We strongly recommend reading this statement in conjunction with the CONSORT 2010, extension to randomised pilot and feasibility trials, Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

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Tailored exercise and manual therapy versus standardized exercise for patients with shoulder subacromial pain: a feasibility randomized controlled trial (the Otago MASTER trial)

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Tailored exercise and manual therapy versus standardized exercise for patients with shoulder subacromial pain: a feasibility randomized controlled trial (the Otago MASTER trial)

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Abstract

Objectives

The aim of this study was to assess whether it was feasible to conduct a full trial comparing a tailored versus a standardized exercise programme for patients with shoulder subacromial pain.

Design

Two-arm, patient- and assessor-blinded, randomized controlled feasibility trial.

Methods

Twenty-eight participants with shoulder subacromial pain were randomly allocated into one of two intervention groups – tailored or standardized exercise. Participants in the tailored exercise programme received exercises and manual therapy tailored to their scapular and shoulder movement impairments. Participants in the standardized exercise programme received progressive strengthening exercise. The primary outcome measures were (1) the participant recruitment rate; (2) the proportion of participants enrolled from the total number screened; (3) drop-out rates; and (4) adherence to the rehabilitation programme. Other outcome measures were: (5) pain levels; (6) patient specific functional scale (PSFS); (7) the Shoulder Pain and Disability Index (SPADI); and (8) pain self-efficacy. We compared changes in pain and disability scores between groups using a repeated mixed-model analysis of variance. Since this is a feasibility study, we did not adjust alpha for multiple comparisons, and considered 75% CI as the probability threshold at 3-month follow-up. Health-related quality of life was assessed using the Short-Form 12 and quality-adjusted life years (QALYs) were estimated.

Results

The recruitment rate was 3 participants per month, the proportion of participants enrolled was 23%, the drop-out rate was 14%, and the overall adherence to the rehabilitation programme was 85%. No between-group differences were found for most outcome measures. Adverse events (n=2, only in the tailored group) were minor in nature and included skin injury or pain following taping.

Conclusions

Our feasibility trial showed that additional strategies are required for improving recruitment, enrolment and minimizing drop-out of participants into the trial and making it feasible to conduct a full trial.

Ethics

This study was approved by the University of Otago Ethics Committee [H17/080].

Trial registration number

ANZCTR: 12617001405303.

Keywords

Shoulder, rehabilitation, manual therapy, feasibility trial.

Word count

3880

Strengths and limitations of this study

- The protocols used for both intervention arms had detailed information about how to progress each of the included exercises over the intervention period.

- Clinicians received training sessions to familiarize themselves with the protocol and the trial only started after clinicians received the training and considered themselves familiarized with interventions from both arms.

- Efficiency of recruitment and enrolment, participant adherence and retention were exposed as limitations of the study design, however most participants did adhere to the rehabilitation programme, and the drop-out rate was within *a priori bounds*.

- Session duration is not representative of current practice in New Zealand, limiting generalisability, however, current practices should not restrain research from testing new intervention practices that may deliver better outcomes for patients with shoulder disorders.

Tailored versus standardized exercise for patients with shoulder subacromial pain: a feasibility randomized controlled trial (the Otago MASTER trial)

Introduction

Shoulder pain is the third most common musculoskeletal complaint, with a one-year prevalence of 18.1%.[1] This high prevalence in combination with the significant disability caused by shoulder pain results in high burden – the average annual cost of shoulder subacromial pain has been estimated at $4,139 per patient, in Sweden,[2] and in NZ costs for shoulder injuries totalled NZ$14 million/year in on average from 2005 to 2013.[3] Shoulder subacromial pain is defined as pain at the top and lateral part of the shoulder joint, may spread to the neck and elbow, and is worsened by overhead activity.[4] It has a slow recovery,[5] with only 50% of new episodes presenting full recovery within 6 months.[6]

Best evidence recommends exercise therapy be prescribed for patients with shoulder subacromial pain.[7 8] However, the strength of evidence supporting this recommendation is limited and findings from two large trials found exercise therapy did not provide additional benefit over usual care.[9 10] On the other hand, a recent systematic review and network meta-analysis suggested that, among other interventions, exercise and manual therapy are likely to be effective in the short-term for pain and function outcomes.[11] Currently, it is uncertain: (1) if exercise therapy is more effective than placebo; (2) which form of exercise therapy is likely to be more effective; (3) whether exercise combined with manual therapy is likely to be more effective than exercise alone.

There is conflicting evidence in the literature regarding effectiveness of exercise therapy when compared to placebo (i.e. detuned ultrasound or detuned laser therapy). One trial found exercise and manual therapy are no different to detuned ultrasound;[12] while another trial found exercise therapy to be more effective than detuned laser therapy.[13] The last Cochrane Review recommended future trials to compare exercise interventions with placebo.[14]

With regards to the type of exercise, one large trial reported specific exercise programme (targeting rotator cuff and scapular muscles) to be more effective than a generic strengthening exercise programme.[15] However, findings from a systematic reviews suggest limited evidence regarding the effectiveness of specific resistive exercise when compared to general strengthening exercise.[16] Two recent reviews suggested future trials to compare different types, dose or duration of exercise therapy regimens.[16 17]

The role of manual therapy in the management of patients with shoulder subacromial pain is unclear and debated in the literature.[17] There are conflicting recommendations from previous trials and reviews in the topic.[11 14 17 18] Evidence from trials on other musculoskeletal disorders suggest that including manual therapy led to better clinical outcomes when compared to corticosteroid injection or wait-and-see in the management of other musculoskeletal disorders (e.g. tennis elbow),[19] or usual care when managing patients with hip or knee osteoarthritis.[20] A recent systematic review and network meta-analyses suggest exercise and manual therapy are likely to have small to moderate treatment effects on patients with shoulder subacromial pain, but the level of certainty was low.[11]

Together, findings from those previous trials and systematic reviews suggest it is unclear whether exercise therapy (when combined or not with manual therapy) is effective for managing patients with shoulder subacromial pain in comparison with placebo or usual care. It is also unclear which form of exercise therapy interventions are more likely to be effective for improving pain and function in those patients. The aim of our full study is to assess the clinical- and cost-efficacy of a tailored exercise

programme versus a standardised exercise programme versus usual care for the treatment of shoulder subacromial pain.

Prior to conducting a fully-powered randomized controlled trial (RCT), we conducted a feasibility trial to assess: (1) the participant recruitment rate; (2) the proportion of participants enrolled from the total number screened; (3) adherence to the exercise programmes; (4) drop-out rates; (5) preliminary estimates of adverse events; (6) preliminary estimates of intervention effects in order to inform the sample size of the fully-powered RCT; and (7) the feasibility of collecting costs-related data within the trial.

Methods

Trial design

The Management of subacromial disorders of the shoulder (MASTER) trial is a two-arm, patient- and assessor-blinded, feasibility randomized controlled trial. Participants were randomly allocated into one of two intervention groups: a standardized or a tailored exercise programme.

We followed the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement: extension to randomised pilot and feasibility trials.[21] In addition, we followed the Template for Intervention Description and Replication (TIDieR) checklist and guide.[22] The study protocol was prospectively registered with the Australian and New Zealand Clinical Trials Registry (ANZCTR: 12617001405303) and published.[23] This study was approved by the University of Otago Ethics Committee [H17/080].

Participants

We recruited participants with shoulder subacromial pain, aged from 18 to 65 years old, from within the Dunedin area (New Zealand) through newspaper advertisements. Participants were screened by a musculoskeletal physiotherapist, following the British Elbow and Shoulder Society (BESS) guidelines.[4] Given the challenges in diagnosing patients with shoulder pain and the low sensitivity of most clinical tests for the shoulder disorders,[24] we widened the criteria proposed by BESS and added resisted lateral rotation and shoulder abduction.[25]

The BESS guidelines screen for red flags (e.g. tumour, unreduced dislocation, acute rotator cuff tear, infection), shoulder pain with cervical spine origin, shoulder instability, acromioclavicular joint disease, or adhesive capsulitis.[4] Participants were included if they presented a positive finding on one of the following tests: (1) Painful arc movement during shoulder flexion or abduction; (2) Jobe's test;[4] or (3) pain on resisted lateral rotation or abduction.[25]

We excluded participants with a history of shoulder dislocation, shoulder subluxation, shoulder surgery and cervical surgery within the last 6 months,[26] participants with any kind of symptoms of systematic inflammation or disease, signs of paraesthesia in the upper extremities, hemiplegic shoulder pain, frozen shoulder, or positive clinical signs of full thickness rotator cuff tear.[27]

All participants provided written consent prior to taking part in the study.

Interventions

Participants in both groups received 16 individual, face-to-face sessions, each lasting for approximately 60 min, over an 8-week period. Details of interventions can be found in the published protocol.[23] Participants were encouraged to not undertake any other treatment during the trial, but could do so, should they wish to pursue that. We asked participants to report any concurrent treatment during the trial.

Participants performed 8 exercises per session, plus three stretches (control group) or up to three manual therapy techniques (tailored group). To enhance internal validity of the trial, the number of exercises and duration of sessions were planned to be equivalent. The intensity of strengthening exercises was monitored using a modified Borg scale.[28] The Borg scale is valid tool for measuring exertion during resistance training.[29 30]

Tailored exercise programme: participants allocated to the tailored exercise programme received exercises focusing on restoring normal movement pattern and the dynamic stability of the

scapulothoracic and glenohumeral joints,[31 32] in addition to manual therapy techniques for restoring shoulder and scapular movement[33] and progressive resistance training of impaired muscles.[32 34] Theoretically, this intervention should lead to better clinical outcomes given it targets specific neuromuscular and join impairments presented by the patient.

Standardized exercise programme: participants allocated to this group received progressive resistance training for all scapular and shoulder muscles and a stretching exercise programme.[35] This intervention focused on restoring muscle flexibility and strength.

Primary outcome measures

The primary outcome measures were: (1) the participant recruitment rate, measured as number of participants enrolled per month; (2) the proportion of participants enrolled from the total number screened, with reasons for exclusion; (3) drop-out rates, expressed as a percentage of the total number of participants enrolled; and (4) adherence to the exercise programme, measured as number of sessions attended as a percentage of the total number of planned sessions.

Other outcome measures

Other outcomes were collected via face-to-face interviews. When selecting outcome measures to use for this feasibility trial, we considered the patient-reported outcome measures intended as the primary and secondary outcomes to be used in the main trial. Hence, the outcome measures were:

(1) Pain intensity (at rest, during arm movement and average pain during the last 7 days) measured by a numeric pain scale.[36] The numeric pain scale is a reliable and responsive tool when used with patients with shoulder pain.[37] The minimal clinically important difference (MCID) for the 10-point numeric pain scale in patients with shoulder pain is 1.1 points.[37] High scores represent worse outcomes.

(2) The Patient Specific Functional Scale (PSFS). The PSFS measures disability and is a valid, reliable and responsive tool for assessing patients with shoulder pain.[38] The MCID for the PSFS is 1.3 (for small changes), 2.3 (medium changes) and 2.7 (large changes) in patients with a range of musculoskeletal disorders.[39] Low scores represent worse outcomes.

(3) The Shoulder Pain and Disability Index (SPADI) total score (including the pain and disability subscales).[40] The SPADI presents acceptable construct validity and responsiveness in patients with shoulder pain.[41] According to a systematic review, the MCID for the SPADI total score ranges from 8 to 13.[42] High scores represent worse outcomes.

(4) The pain self-efficacy questionnaire.[43] The pain self-efficacy questionnaire is an established and commonly used tool for assessing self-efficacy in individuals with pain.[44] The MCID for the pain self-efficacy questionnaire is 9 points for patients with low back pain.[45] Low scores indicate low levels of self-efficacy when dealing with pain.

We assessed safety by recording all adverse events, both related and unrelated to interventions, in each group. The literature suggests adverse events to exercise therapy might be common, but not serious.[46] Potential adverse reactions to interventions may include muscle soreness or increased pain around the shoulder joint. The physiotherapist recorded any adverse reactions to interventions, including duration and severity of adverse reaction to treatment, and how the adverse reaction was managed. We included in the report the total number of participants who reported adverse events, relatedness to interventions, and the duration and severity of the adverse reactions. In the small

sample of this feasibility trial, we did not expect to observe a representative number of adverse events, so did not undertake statistical comparisons.

Economic outcomes

Health-related quality of life was assessed using the Short-Form 12 (SF-12v2) questionnaire.[47] To allow the calculation of health utility values for the economic evaluation the SF-12v2 was converted to a six-dimensional health state classification (SF-6D).[48] Health utility is a preference-based measure of overall health-related quality of life, on a scale from 0 (equivalent to death) to 1 (full health). Quality-adjusted life years (QALYs) were estimated for each participant by calculating the area under the curve (the product of utility values by time) from baseline to 12-week follow-up. We calculated the mean QALYs for each group and adjusted for baseline utility scores to minimize any bias due to chance of baseline imbalance between the groups.

We adapted the Otago Cost and Consequences Questionnaire (OCC-Q) to shoulder disorders and used the adapted questionnaire to capture healthcare use and other non-healthcare costs (e.g., time off work).[49] The OCC-Q is a validated patient-administered questionnaire developed for osteoarthritis that has demonstrated accuracy and agreement with administrative databases in the New Zealand healthcare system.[49] The OCC-Q was administered at baseline and 12-week time points. Costs are expressed as 2019 NZ dollars, exclusive of Goods and Services Tax.

Sample size

Given this is a feasibility trial, we did not design it to assess the efficacy of the experimental intervention.[50 51] Whitehead et al.[52] recommend the sample size of a feasibility study should be estimated based on the expected range for the effect size, the power and alpha (both established *a priori*), and the total number of arms of treatment planned for the full trial.[52]

Whitehead et al.[52] estimated the sample size based on standardized differences of different magnitudes (i.e. extra small, small, medium and large). To estimate sample size, we used the Shoulder Pain and Disability Index (SPADI) as the presumed primary outcome measure for the full trial and assumed a minimum clinically important difference of 8 points,[53] with a standard deviation of 24 points.[53] This represents a standardized effect size of 0.3. We considered a full trial with power of 80%, two-tailed between-group comparison, and alpha at 0.05. Therefore, the minimum sample size for this feasibility RCT is 10 participants per arm of treatment, assuming a medium effect size.[52] Assuming a 20% loss to follow-up,[54] we aimed for a minimum sample size of 25 participants.

Randomization

Sequence generation, allocation concealment, implementation

Participants were allocated (1:1 ratio) into one of the intervention groups (i.e., tailored physiotherapy or standardized physiotherapy) through blocked randomization (with blocks of 4). The randomisation schedule was computer-generated by a research administrator not involved with delivering the interventions, and concealed in numbered, sealed, and opaque envelopes. A research administrator provided the envelope to the clinician delivering the interventions.

Blinding

Participants and outcome assessors were blinded to group allocation. Clinicians delivering the interventions were not blinded to group allocations due to nature of interventions.

Time points

Outcome measures were recorded at baseline and at the 4th, 8th, and 12th weeks after baseline.

Statistical analysis

We used descriptive statistics analyses for presenting: (1) recruitment rates; (2) proportion of participants enrolled from the total number screened; (3) drop-out rates; (4) adherence to the exercise programme; and (5) adverse events and for reporting economic outcomes. The primary and secondary analyses were intention-to-treat and involved all patients who were randomly assigned. All statistical analysis were conducted using R.[55]

We used linear mixed-effect models to obtain estimates of treatment effects. We conducted within- and between-group comparisons using an independent linear mixed-effect model for each outcome measure (i.e., numeric pain rating scale, PSFS, SPADI pain score, SPADI disability score, SPADI total score, and Pain Self-efficacy). This feasibility trial was not powered to detect superiority; however, we assessed the magnitude of mean treatment effects for pain and disability in relation to clinically important changes. This was done for informing the choice of primary outcome measure to be used in the main trial and thus informing the sample size calculation for the main trial.[56] When running linear mixed-effect models, we estimated marginal means and their respective 75% confidence intervals. For that reason, we did not adjust alpha for multiple comparisons. This statistical approach is considered appropriate for feasibility or exploratory studies.[57]

When conducting within-group comparisons, group allocation (tailored and standardized exercise groups) and 'time-point' (baseline, 4th, 8th week and 12th week) were considered as fixed-effects. Participants were considered as random effects. Post-hoc analyses were conducted for comparing changes in scores between "baseline vs 4 weeks", "baseline vs 8 weeks", and "baseline vs 12 weeks".

When conducting between-group comparisons, group allocation (tailored and standardized exercise groups) and 'time-point' (4th, 8th week and 12th week) were considered as fixed-effects. Participants were considered as random effects. Baseline measurements were considered as covariates. Post-hoc analyses were conducted for comparing scores between groups at each time point (i.e., 4, 8 and 12 weeks).

To help inform whether it is worthwhile conducting the full trial, it is recommended that preliminary between-group comparisons be performed at the feasibility trial stage.[58 59] For that, confidence interval ranges other than 95% are recommended when assessing between-group differences from feasibility trials (e.g. 75% CI in addition to the mean difference estimate).[58] For the purposes of this study, we considered 75% CI as the probability threshold for between-group analyses.[58] Such information will be considered when assessing whether to conduct the full trial.[58 59]

Missing data

Linear mixed-effect models can handle missing data. For descriptive analysis, in case of missing data, we explored pattern of missingness using the "mi" package in R.[60] After running such analysis, we accepted that data was missing at random and performed multiple imputation by chained equations using the "mice" package.[61]

Additional analysis

When running the mixed-effect models, we found residuals presented small deviations from the normal distribution. In those cases, it is recommended to conduct robust mixed-effect models and report estimates from both models (i.e., standard and robust mixed-effect models).[62] We implemented the robust mixed-effect models using the "rlmer" function from WRS 2 package.[62] The robust models had the same input data as the standard mixed-effect models (described above) and yielded similar estimates of treatment effects to those obtained with standard mixed-effect models. For that reason, we report in the main text the estimate effects obtained through the mixed-effect models and reported the estimate effects obtained through the robust mixed-effect models in the Supplementary material 1.

Results

Recruitment and flow of participants

The recruitment flow and randomization process are presented in Figure 1. The trial started recruiting on 19th January 2018 and completed recruitment on the 23rd of October 2018. The trial ended after recruiting the minimum number of participants as per sample size calculations.

Figure 1

A total of 117 individuals showed interest in taking part in the study and completed telephone screening; 51 were excluded at that screening stage. The main reasons for exclusion were inability to commit to the study, no response after receiving the information sheet or not meeting the inclusion criteria.

Fifty-three participants were physically screened, with 24 participants excluded following physical screening. Reasons for being excluded included (with some participants meeting more than one exclusion criteria): not presenting positive tests to physical examination of the shoulder (n = 12), symptoms caused by neck disorder (n = 7), history of subluxation (n = 1), frozen shoulder (n = 2), AC joint involvement (n = 4), inflammatory disease (n = 3). Following physical screening, 28 participants were eligible for randomization.

Participants' characteristics

The demographics and clinical characteristics of participants are presented in Table 1.

Table 1. Baseline characteristics of 28 participants. Data reported as mean and standard deviation or as count and percentage.

Variables	All participants (N=28)	Standardized exercise group (N=15)	Tailored training group (N=13)
Age (years)	43.89 (9.6)	43.7 (11.7)	44.1 (6.8)
Women	13 (44%)	5 (41%)	4 (40%)
Weight (kg)	82.4 (13.2)	79.4 (12.6)	86.0 (13.5)
Height (cm)	173.2 (10.0)	171.3 (9.7)	175.7 (10.3)
BMI (kg/m2)	27.3 (4.2)	27.2 (4.5)	27.4 (3.9)
Hand dominant, right side	23 (82%)	11 (73%)	12 (92%)
Affected side, dominant shoulder	17 (60%)	10 (66%)	7 (53%)
Shoulder pain duration (months)	49.0 (76.3)	28.3 (28.4)	66.9 (99.8)
Previous history of shoulder pain	6 (21%)	2 (13%)	4 (31%)
Previous treatment of shoulder	9 (32%)	5 (33%)	4 (31%)
Positive painful arc test	86%	80%	92%
Positive Jobe's test	78%	86%	69%
Positive painful resisted external rotation	28%	26%	30%
Positive painful resisted abduction	30%	40%	16%
Pain at rest	2.0 (1.8)	1.6 (1.6)	2.4 (1.9)
Pain during movement	5.3 (2.0)	5.2 (1.9)	5.5 (2.2)
Pain within the last week	4.2 (2.1)	4.0 (2.3)	4.4 (1.9)
Pain self-efficacy	48.0 (9.6)	50.5 (7.2)	45.1 (11.4)
PSFS	4.6 (1.8)	5.0 (1.7)	4.2 (1.8)
SPADI Total	35.5 (15.1)	33.8 (13.3)	37.5 (17.3)
SPADI Pain	51.4 (15.2)	49.8 (15.8)	53.2 (15.0)
SPADI Disability	25.7 (17.1)	24.0 (13.8)	27.7 (20.7)

Abbreviation: PSFS: Patient Specific Functional Scale; SPADI: Shoulder Pain and Disability Index.

Outcomes and estimation

Primary outcome measures

Findings for primary outcome measures are presented in Table 2. The proportion of participants enrolled from the number of participants screened was 23%. The participant recruitment rate (number of participants recruited per month of active recruitment) was 3. The drop-out was 14% for all participants enrolled in the trial. Four participants allocated to the standardized intervention dropped out. One participant dropped out of the study due to relocation to another city. The other three participants withdrew before initiating physiotherapy intervention, the reasons for dropping out were: not able to commit to the study (n=2) and not wishing to wait for the start of interventions (n=1). All participants allocated to the tailored exercise programme completed the trial. The adherence to the exercise programme was 85% for all participants combined, with 73% for participants allocated to the standardized group and 100% for participants in the tailored group.

Table 2. Descriptive statistics for primary outcome measures.

Outcome	All participants (n=28)	Standardized group (n=15)	Tailored group (n=13)
Proportion of participants enrolled from total screened	23%	--	--
Recruitment rate (recruited per month)	3	--	--
Drop-out rates	14%	26%	0%
Adherence to the exercise programme (percentage of sessions attended)	85%	73%	100%

Other outcome measures

The descriptive mean scores for pain, disability and pain self-efficacy are presented in Table 6. The within-group changes are presented in the supplementary material 2. The estimated marginal mean for between-group differences and their respective 75% confidence intervals are presented in the supplementary material 2. The estimated marginal means obtained with the standard and robust mixed-effect analyses are presented in the supplementary material.

Table 3. Participants' scores for pain, disability, and function at each time point (mean and standard deviation).

	Standardized (n=15)				**Tailored (n=13)**			
	Baseline	4 weeks	8 weeks	12 weeks	Baseline	4 weeks	8 weeks	12 weeks
Pain at rest	1.67 (1.59)	0.9 (0.9)	0.3 (0.5)	0.7 (0.8)	2.4 (1.9)	1.5 (1.5)	0.4 (0.6)	0.4 (0.5)
Pain during movement	5.2 (1.9)	1.3 (0.9)	1.0 (0.5)	1.3 (1.2)	5.5 (2.2)	2.3 (2.2)	1.5 (1.9)	1.1 (1.1)
Pain last week	4.0 (2.3)	1.9 (0.9)	1.3 (0.7)	1.4 (1.2)	4.4 (1.9)	1.8 (1.3)	1.1 (0.8)	1.0 (0.8)
PSFS	5.0 (1.8)	7.1 (1.9)	7.7 (1.3)	6.5 (2.9)	4.2 (1.8)	7.0 (2.2)	7.8 (2.1)	7.2 (2.8)
SPADI Pain	49.8 (15.8)	12.8 (4.6)	17.5 (11.3)	16.8 (15.7)	53.2 (15.0)	15.8 (9.6)	18.6 (12.8)	18.6 (11.9)
SPADI Disability	24.0 (13.9)	9.4 (7.1)	7.0 (6.1)	7.5 (10.0)	27.7 (20.7)	15.8 (11.8)	5.9 (9.3)	6.5 (11.9)
SPADI Total	33.9 (13.3)	16.1 (6.1)	11.2 (6.9)	11.2 (12.0)	37.5 (17.3)	22.0 (13.2)	10.8 (8.4)	11.2 (11.0)
Pain Self-Efficacy	50.5 (7.20)	55.9 (3.2)	55.0 (4.0)	55.9 (5.8)	45.1 (11.4)	53.5 (7.3)	56.2 (5.2)	57.5 (3.4)

PSFS: Patient Specific Functional Scale.

Economic outcomes

The mean QALYs and costs regarding visits to healthcare practitioner, healthcare tests or treatment or pain medications at 12 weeks follow-up are presented in Table 4.

Table 4. Total costs (in 2019 NZ$) and health outcomes at 12-week follow-up.

	Standardized group (n=15)	Tailored group (n=13)
Cost outcomes		
Healthcare practitioner		
GP	0	480
Physiotherapist	26,400	31,650
Chiropractor	0	150
Acupuncturist	0	0
Massage Therapist	0	225
Healthcare tests / treatment		
X-rays	0	137
Other	0	40**
Cortisone injection	0	0
Medications		
Paracetamol	5	5
NSAID*	0	0
COX-2 inhibitors	0	0
Travel costs	1431	830
Productivity cost	16	1817
Total health system cost	26,405.00	32,687.10
Total societal cost	27,852.27	35,334.04
Health outcomes		
QALYs (SD)	0.17 (0.02)	0.18 (0.02)

**dressings. SD = standard deviation.

Harms

All adverse events were considered minor events. A total of 2 adverse reactions were reported, all by participants allocated to the tailored group (Table 5). Adverse reactions skin injury following taping of the shoulder and increase in shoulder pain following taping of the shoulder.

Table 5. Adverse reactions reported by participants following treatment.

	Total	Standardized	Tailored
Taping: skin injury	1	0	1
Taping: increase in shoulder pain	1	0	1
Total	2	0	2

Discussion

This trial assessed the feasibility of conducting a full trial that will compare two forms of exercise therapy for patients with shoulder subacromial pain (one tailored and one standardized exercise programme). Overall, our findings suggest it is feasible to conduct the full trial given that most participants adhered to the exercise programme, and the drop-out rate was within *a priori* bounds. However, prior to conducting the full trial, few amendments to the design are required.

We identified limitations that must be addressed when designing the full trial. Our recruitment rate was lower than previous full trials[8 63] but similar to a previous feasibility trial.[64] Our ability to enrol participants into the trial during the 9-month period of recruitment was limited by the number of clinicians involved with the study. That impacted on recruitment rate and that can be addressed in the future trial by having a multi-centre design. For the present study, the clinic responsible for delivering the interventions limited the number of participants that could be treated to a maximum of 10 at any given time. That impacted on flow of participants in the trial and prevented us from continuously enrolling participants. Therefore, we had to recruit participants in three stages. Some participants opted to drop-out after being screened for eligibility and notified that there would be a waiting period for interventions to start.

We recruited participants through a local newspaper. This may explain why most of our participants presented mild to moderate pain intensity. Participants in our study presented lower pain or function scores compared to those from previous full trials [8 10 65 66]. For the full trial, we plan to adopt a multi-modal recruitment strategy, including general practice clinics, social media, and waiting list from local hospitals. Such strategy may help to optimize recruitment rate and recruit patients with higher levels of shoulder pain or disability.

Our sample presented similar scores for pain and slightly lower scores for disability at baseline compared to a large trial with participants with shoulder subacromial pain.[12] Participants in both groups were exposed to active interventions and presented similar changes in pain and function scores over time. The magnitude of changes in pain scores at 12 weeks were greater than those reported by participants exposed to exercise therapy or placebo intervention reported by that large trial.[12] Feasibility and pilot trials are notorious for their imprecise estimates of treatment, given their small sample sizes.[67] For the full trial, we will include a control arm (e.g., an inactive control such as de-tuned therapeutic ultrasound or laser, or usual care) to be able to estimate the effect of standardized or tailored interventions on clinical outcomes. This strategy has been successfully used before.

When designing the future trial, we will consider a multi-centre design to ensure the minimum sample size required for the full trial is met. Multi-centre trials tend to provide treatment effects that are smaller when compared to single-centre trials and be more pragmatic than smaller trials. It is suggested that the estimate treatment effect observed in a multi-centre trial is closer to those we would observe in clinical practice.[68-70] For those reasons, multi-centre trial are more relevant and useful for clinicians, patients and policy-makers than single centre trials.

Our findings helped to identify the primary outcome measures to use in the full trial. According to a recent Delphi study, trials on shoulder disorders should assess the following domains: pain, physical functioning, global assessment of treatment success and health-related quality of life.[71] Based on our findings, pain during arm elevation presented the largest changes from baseline to 12-week follow-up for both groups. Recently, it has been recommended that movement-evoked pain should be used for assessing musculoskeletal pain.[72] Our findings also suggested important within-group changes for PSFS and SPADI scores and either of those outcome measures could be used in the full trial. The

advantage of PSFS is that it assesses tasks that are especially relevant for a given participant,[40] while, SPADI suffers the limitation of fixed-item instruments, where some items in the questionnaire may not be relevant to a given participant.[40] Based on that, PSFS should be considered as a primary outcome measure in the full trial. In this feasibility study, we did not assess the "global assessment of treatment success" and the future trial should include an outcome measure assessing that construct. We assessed health-related quality of life using the Short-Form 12 (SF-12v2) questionnaire and that should be included in the full trial. When designing the final trial, we will follow the most current recommendations and future work by the Outcome Measures in Rheumatology (OMERACT) Shoulder Working Group.[71 73]

Strengths and limitations

The trial design had some notable strengths. The protocols used for both intervention arms had detailed information about how to progress with exercises over the intervention period. Clinicians received training sessions to familiarize themselves with the protocol and the trial only started after clinicians received the training and considered themselves familiarized with interventions from both arms. We adopted clinical outcomes that are recommended for trials recruiting patients with shoulder disorders.[73] Despite the longer duration of interventions, compared to current practice in New Zealand and other countries, participants adhered to both exercise programmes. The number of participants dropping out was low. In the standardized exercise group, there was a larger number of participants (n = 3) dropping out after enrolling than the tailored group. The drop-out occurred before starting interventions. Findings from the full trial will help to identify whether a tailored or standardized exercise programme are more effective than a control intervention, reducing the socio-economic burden of shoulder subacromial pain.

One criticism of our design is the duration of the interventions (i.e., sessions lasting for 40-60 min) which is not representative of current practice in New Zealand. On the other hand, findings from one trial suggested higher dosage of exercise therapy led to better clinical outcomes.[74] In addition, current practices should not restrain research from testing new interventions that may deliver better care for patients with shoulder disorders. While our trial will not compare different exercise therapy dosages, it will add valuable information regarding the effect of different forms of exercise therapy delivered at equivalent dosage. In addition, as per our protocol, our nested process evaluation study was conducted parallel to this feasibility trial and will provide more detailed information regarding the participants' and clinicians' perceptions of the interventions tested in this feasibility trial. We have conducted a focus group with clinicians and individual interviews with patients who took part in the study to assess their perceptions about the interventions received. These findings will be prepared for publication as separate manuscripts. The information from the current study and the nested process evaluation will be used for improving the design of the full trial.

Conclusions

Our feasibility trial showed that additional strategies are required for improving recruitment, enrolment and minimizing drop-out of participants into the trial. By adopting additional strategies and addressing some of the limitations identified through this feasibility study, it is likely feasible to conduct a full trial assessing the efficacy of a tailored exercise programme.

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Declarations

Patient and Public Involvement

Patients and or public were not involved. At the time of the planning and designing of this study, we did not have the network and contact in place for this. Results of this study will be disseminated to study participants by inviting them to join an open-seminar in which the results of the study will be presented. In addition, we will prepare a short report with the main findings of the study and distribute this by e-mail to participants. When planning the full trial, we will engage with patient and public representatives to ensure their input is considered at the early stages of the design.

Data collection, storage and sharing

We stored participants' data on a secure local server and used unique identification number on follow-up questionnaires. To protect participants' privacy, all identifying information will be stored separately, and deleted following the conclusion of the trial. We will not share or report identifying information. The datasets generated during the study will be available from the corresponding author on reasonable request.

Confidentiality

Only the research team had access to personal information. We will use group mean data to present findings from the study. This will protect confidentiality before, during, and after the trial. We will safely store the data for 10 years.

Adverse event management

The risk of a serious adverse event related to the intervention is minimal. We maintained a Data Monitoring Committee (Centre for Health, Activity and Rehabilitation Research—University of Otago) to assess whether it is necessary to report the adverse event to the trial sponsor, and Ethics Committee.

Protocol amendments

There were no changes to protocol during the implementation of this feasibility trial.

Competing interests statement

None declared.

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research was conducted during tenure of The Sir Charles Hercus Health Research Fellowship of the Health Research Council of New Zealand (Grant number: 18/111) awarded to DCR.

The Health Research Council – New Zealand had no role in the design of the trial and will have no role in its execution, data analysis and interpretation, or on the submission of the studies for publication.

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Captions

Figure 1. Flow of participants in the trial.

Table 4. Baseline characteristics of 28 participants. Data reported as mean and standard deviation or as count and percentage.

Table 5. Descriptive statistics for primary outcome measures.

Table 6. Participants' scores for pain, disability, and function at each time point (mean and standard deviation).

Table 7. Total costs (in 2019 NZ$) and health outcomes at 12-week follow-up.

Table 5. Adverse reactions reported by participants following treatment.

Authors' contributions

DCR and ZJT conceived the research question. DCR was responsible for the design of the trial and is the guarantor. ZJT and GS contributed to the design of interventions. JHA provided guidance on the design the trial and economic analysis. RW provided guidance on economic analysis. DCR led efforts for securing funding, with the contributions from ZJT, GS and JHA. All authors revised and approved the protocol for the study. All authors revised the manuscript for important content and approved the final version.

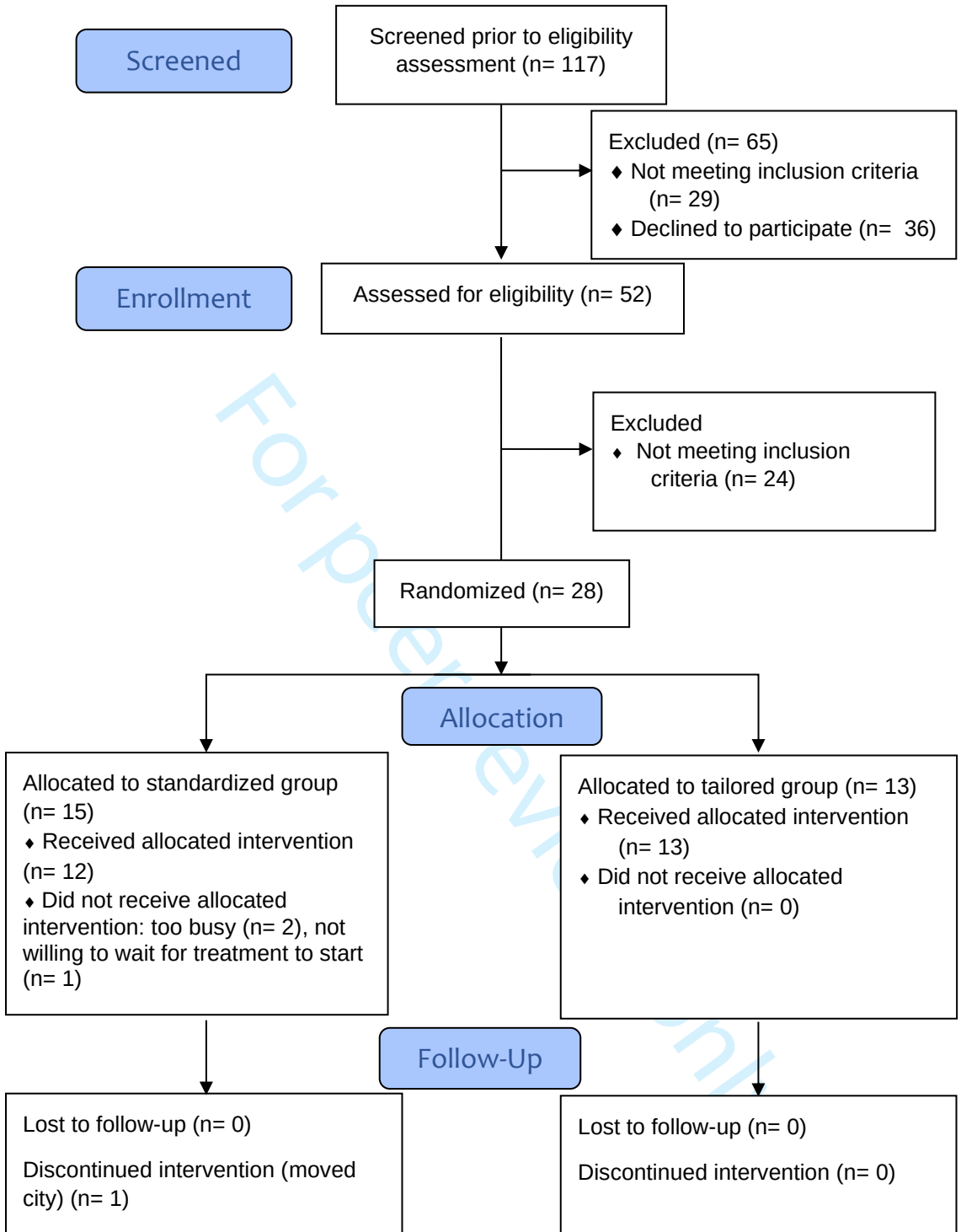

Figure 1. Flow of participants in the trial.

Centre for Health, Activity, and Rehabilitation Research

Supplementary material 1

The Otago MASTER Trial

Authors: Daniel Cury Ribeiro, Zohreh Tangrood Jafarian, Ross Wilson, Gisela Sole, J. Haxby Abbott

Contents

University of Otago
Te Whare Wānanga o Otāgo
New Zealand

Centre for Health, Activity, and Rehabilitation Research

1. Overview

Below, we present the estimated marginal means, standard error (SE) and 95% confidence intervals (CI) for estimates when analyzing data using the mixed-effect model, the robust mixed-effect model.

The estimated marginal means and standard errors are very similar between the standard and robust mixed-effect models for all outcomes. For that reason, we presented in the manuscript findings from the standard mixed-effect model in the main manuscript.

2. Pain at rest

2.1. Mixed-effect model

Group	Time point	EMM	SE	95% CI
Standardized	2	0.8	0.2	0.3 to 1.2
Tailored	2	1.3	0.2	0.9 to 1.7
Standardized	3	0.4	0.2	0.0 to 0.8
Tailored	3	0.3	0.2	-0.1 to 0.7
Standardized	4	0.4	0.2	0.0 to 0.8
Tailored	4	0.3	0.2	0.0 to 0.7

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

2.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	0.8	0.2	0.3 to 1.2
Tailored	2	1.2	0.2	0.8 to 1.6
Standardized	3	0.4	0.2	0.0 to 0.8
Tailored	3	0.3	0.2	-0.1 to 0.7
Standardized	4	0.4	0.2	0.0 to 0.8
Tailored	4	0.3	0.2	-0.1 to 0.7

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

3. Pain during movement

3.1. Mixed-effect model

Group	Time point	EMM	SE	95% CI
Standardized	2	1.5	0.4	0.7 to 2.3
Tailored	2	2.6	0.4	1.9 to 3.4
Standardized	3	0.9	0.4	0.1 to 1.7
Tailored	3	1.5	0.4	0.7 to 2.2
Standardized	4	1.0	0.4	0.2 to 1.9
Tailored	4	1.1	0.4	0.3 to 1.9

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

3.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	1.5	0.3	0.8 to 2.1
Tailored	2	2.5	0.3	2.0 to 3.1
Standardized	3	0.8	0.3	0.2 to 1.4
Tailored	3	1.2	0.3	0.6 to 1.7
Standardized	4	1.0	0.3	0.4 to 1.6
Tailored	4	0.9	0.3	0.4 to 1.5

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

4. Pain last week

4.1. Mixed-effect model

Group	Time point	EMM	SE	95% CI
Standardized	2	1.9	0.3	1.3 to 2.4
Tailored	2	2.0	0.2	1.5 to 2.5
Standardized	3	1.4	0.3	0.8 to 1.9
Tailored	3	1.0	0.2	0.5 to 1.5
Standardized	4	1.1	0.3	0.6 to 1.6
Tailored	4	0.9	0.2	0.4 to 1.4

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

4.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	1.8	0.2	1.3 to 2.3
Tailored	2	1.8	0.2	1.4 to 2.3
Standardized	3	1.4	0.2	0.9 to 1.9
Tailored	3	1.0	0.2	0.6 to 1.5
Standardized	4	1.1	0.2	0.6 to 1.6
Tailored	4	0.9	0.2	0.4 to 1.3

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

5. SPADI Pain

5.1. Mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	14.0	3.1	7.8 to 20.3
Tailored	2	17.6	2.9	11.7 to 23.5
Standardized	3	18.1	3.1	11.9 to 24.4
Tailored	3	18.8	2.9	12.4 to 23.9
Standardized	4	13.9	3.1	7.7 to 20.2
Tailored	4	18.8	2.9	12.4 to 23.9

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

5.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	14.0	2.7	8.6 to 19.4
Tailored	2	17.6	2.5	12.5 to 22.6
Standardized	3	16.7	2.7	11.3 to 22.0
Tailored	3	17.1	2.5	12.1 to 22.0
Standardized	4	13.9	2.7	8.5 to 19.3
Tailored	4	16.3	2.5	11.3 to 21.3

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

6. SPADI Disability

6.1. Mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	10.6	2.6	5.4 to 15.8
Tailored	2	16.1	2.4	11.3 to 20.9
Standardized	3	5.8	2.6	0.6 to 11.0
Tailored	3	4.8	2.4	0.1 to 9.6
Standardized	4	4.7	2.6	-0.5 to 9.9
Tailored	4	5.4	2.4	0.6 to 10.2

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

6.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	10.3	1.5	7.3 to 13.4
Tailored	2	13.8	1.4	10.9 to 16.7
Standardized	3	5.6	1.5	2.5 to 8.6
Tailored	3	3.2	1.4	0.3 to 6.0
Standardized	4	4.4	1.5	1.4 to 7.5
Tailored	4	3.7	1.4	0.9 to 6.5

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

7. SPADI Total

7.1. Mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	17.4	2.4	12.6 to 22.2
Tailored	2	22.9	2.2	18.4 to 27.4
Standardized	3	10.8	2.4	5.9 to 15.5
Tailored	3	9.7	2.2	5.3 to 14.2
Standardized	4	8.4	2.4	3.6 to 13.2
Tailored	4	10.1	2.2	5.6 to 14.5

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

7.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	17.2	2.0	13.2 to 21.2
Tailored	2	20.6	1.9	16.8 to 24.3
Standardized	3	10.4	2.0	6.3 to 14.4
Tailored	3	8.7	1.9	5.0 to 12.4
Standardized	4	8.3	2.0	4.2 to 12.3
Tailored	4	8.9	1.9	5.9 to 12.6

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

8. Pain Self-Efficacy

8.1. Mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	54.3	1.0	52.2 to 56.3
Tailored	2	53.7	1.0	51.7 to 55.6
Standardized	3	55.9	1.0	53.9 to 57.9
Tailored	3	57.5	0.9	55.6 to 59.4
Standardized	4	56.9	1.0	54.9 to 58.9
Tailored	4	58.9	0.9	57.0 to 60.8

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

8.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	54.5	0.9	52.7 to 56.2
Tailored	2	54.2	0.8	52.6 to 55.9
Standardized	3	56.2	0.9	54.5 to 58.0
Tailored	3	57.8	0.8	56.2 to 59.4
Standardized	4	57.1	0.9	55.3 to 58.8
Tailored	4	58.6	0.8	57.0 to 60.2

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

9. Patient-specific functional scale

9.1. Mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	7.0	0.6	5.7 to 8.2
Tailored	2	6.9	0.6	5.7 to 9.1
Standardized	3	7.6	0.6	6.3 to 8.9
Tailored	3	7.9	0.6	6.7 to 9.1
Standardized	4	7.2	0.6	5.9 to 8.4
Tailored	4	7.3	0.6	6.1 to 8.4

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

9.2. Robust mixed-effect model

Group	Time	EMM	SE	95% CI
Standardized	2	7.1	0.5	6.0 to 8.2
Tailored	2	6.9	0.5	5.9 to 8.0
Standardized	3	7.6	0.6	6.5 to 8.8
Tailored	3	8.1	0.5	7.1 to 9.1
Standardized	4	7.8	0.6	6.7 to 8.9
Tailored	4	7.8	0.5	6.7 to 8.8

EMM: estimated marginal means. SE: standard error. CI: confidence interval.

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Supplementary material 2

The Otago MASTER Trial

Authors: Daniel Cury Ribeiro, Zohreh Tangrood Jafarian, Ross Wilson, Gisela Sole, J. Haxby Abbott

Below, we present two tables, showing findings for within- and between-group comparisons.

Please note these are estimates from a feasibility trial and should not be used for interpreting effectiveness of interventions included in the trial.

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Table S1. Within-group differences (estimated marginal means and 95% confidence intervals).

	Baseline vs 4 weeks		Baseline vs 8 weeks		Baseline vs 12 weeks	
Outcome	Standardized	Tailored	Standardized	Tailored	Standardized	Tailored
Pain at rest Ω	0.9 (0.1 to 1.6)	1.0 (0.2 to 1.7)	1.3 (0.5 to 2.0)	2.0 (1.3 to 2.7)	1.3 (0.5 to 2.0)	2.0 (1.3 to 2.7)
Pain during movement Ω	3.6 (2.6 to 4.5)*	2.8 (1.9 to 3.8) *	4.2 (3.3 to 5.2) *	4.0 (3.1 to 4.9) *	4.0 (3.1 to 5.0) *	4.4 (3.5 to 5.3) *
Pain last week Ω	2.0 (1.2 to 3.0) *	2.3 (1.4 to 3.2) *	2.5 (1.6 to 3.4) *	3.3 (2.4 to 4.2) *	2.8 (1.9 to 3.7) *	3.4 (2.5 to 4.2) *
PSFS #	-2.1 (-3.4 to -0.7)	-2.6 (-4.0 to -1.3) *	-2.7 (-4.1 to -1.4) *	-3.7 (-5.0 to -2.3) *	-1.3 (-2.6 to -0.9)	-3.0 (-4.3 to -1.7) *
SPADI Pain Ω	35.8 (28.2 to 43.5)	35.2 (27.7 to 42.7)	31.7 (24.1 to 39.4)	34.6 (27.3 to 41.9)	35.9 (28.2 to 43.6)	34.6 (27.3 to 41.9)
SPADI Disability Ω	12.4 (6.0 to 18.8)	9.7 (3.5 to 15.9)	17.2 (10.7 to 23.6)	21.7 (15.7 to 27.8)	18.3 (11.9 to 24.8)	21.2 (15.1 to 27.2)
SPADI Total Ω	16.02 (10.2 to 21.8) *	13.1 (7.5 to 18.7)	22.6 (16.9 to 28.4) *	26.7 (21.3 to 32.1) *	24.0 (19.2 to 30.7) *	26.3 (20.9 to 31.8) *
Pain Self-efficacy #	-3.6 (-6.8 to 0.4)	-7.0 (-10.1 to -3.9)	-5.2 (-8.4 to -2.0)	-11.1 (-14.1 to -8.0)	-5.2 (-9.4 to -3.0)	-12.4 (-15.5 to -9.4) *

Ω = Positive differences indicate clinical improvement. # = Negative differences indicate clinical improvement.
*: within-group change greater than the minimal clinically important difference.

Table S2. Estimated marginal means and standard error for each group, and between-group estimated marginal mean differences and their respective 75% confidence intervals.

	4 weeks			8 weeks			12 weeks		
Outcome	**Standardized (n=15)**	**Tailored (n=13)**	**Mean difference**	**Standardized (n=15)**	**Tailored (n=13)**	**Mean difference**	**Standardized (n=15)**	**Tailored (n=13)**	**Mean difference**
Pain at rest #	0.8 (0.2)	1.3 (0.2)	-0.5 (-0.9 to -0.2)	0.4 (0.2)	0.3 (0.2)	0.1 (-0.3 to 0.4)	0.8 (0.2)	0.3 (0.2)	0.1 (-0.3 to 0.4)
Pain during movement #	1.5 (0.4)	2.6 (0.4)	-1.1 (-1.8 to -0.5)	0.9 (0.4)	1.5 (0.4)	-0.6 (-1.3 to 0.0)	1.2 (0.4)	1.1 (0.4)	0.0 (-0.7 to 0.6)
Pain last week #	1.9 (0.3)	2.0 (0.2)	-0.1 (-0.5 to 0.3)	0.4 (0.3)	1.0 (0.2)	0.4 (-0.1 to 0.8)	1.1 (0.3)	0.9 (0.2)	0.2 (-0.2 to 0.6)
PSFS$^{\Omega}$	7.0 (0.6)	7.0 (0.6)	0.1 (-0.9 to 1.1)	7.6 (0.6)	8.0 (0.6)	-0.3 (-1.3 to 0.7)	7.9 (0.5)	7.3 (0.6)	-0.1 (-1.1 to 0.9)
SPADI Pain #	14.0 (3.1)	17.6 (2.9)	-3.6 (-8.6 to 1.5)	18.1 (3.1)	18.8 (2.9)	0.0 (-5.0 to 5.0)	13.9 (3.1)	18.8 (2.9)	-4.2 (-9.2 to 0.8)
SPADI Disability #	10.6 (2.6)	16.1 (2.4)	-5.5 (-9.7 to -1.3)*	5.8 (2.6)	4.8 (2.4)	1.0 (-3.2 to 5.1)	4.8 (2.6)	5.4 (2.4)	-0.7 (-4.9 to 3.4)
SPADI Total #	14.4 (2.4)	22.9 (2.2)	-5.5 (-9.4 to -1.6)*	10.8 (2.4)	9.7 (2.2)	1.0 (-2.8 to 4.9)	8.8 (2.4)	10.1 (2.2)	-1.6 (-5.5 to 2.2)
Pain Self-efficacy$^{\Omega}$	54.3 (1.0)	53.7 (1.0)	0.6 (-1.1 to 2.3)	55.9 (1.0)	57.5 (0.9)	-1.6 (-3.3 to 0.0)	56.9 (1.0)	58.9 (0.9)	-2.0 (-3.7 to -0.3)*

Ω = Positive differences favours standardized group. # = Negative differences favours tailored group.

*denotes differences between groups.

CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	1, 4
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	4
	2b	Specific objectives or research questions for pilot trial	4
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	5
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	N.A.
Participants	4a	Eligibility criteria for participants	5
	4b	Settings and locations where the data were collected	5
	4c	How participants were identified and consented	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	5, 6
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	6
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	N.A.
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	N.A.
Sample size	7a	Rationale for numbers in the pilot trial	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N.A.
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	7
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	7
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	7

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	7
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	7
	11b	If relevant, description of the similarity of interventions	5, 6
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	8, 9
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	9
	13b	For each group, losses and exclusions after randomisation, together with reasons	10
Recruitment	14a	Dates defining the periods of recruitment and follow-up	9
	14b	Why the pilot trial ended or was stopped	9
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	12
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	13 to 17
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	14to 17
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	17
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	18
	19a	If relevant, other important unintended consequences	N.A.
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	19
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	18 to 19
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	18 to 19
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	18 to 19
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	5
Protocol	24	Where the pilot trial protocol can be accessed, if available	5
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	24 to 25
	26	Ethical approval or approval by research review committee, confirmed with reference number	2

Citation: Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355.

*We strongly recommend reading this statement in conjunction with the CONSORT 2010, extension to randomised pilot and feasibility trials, Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.