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Clinical science

Feasibility of conducting a cohort randomized controlled trial assessing the effectiveness of a nurse-led package of care for knee pain

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Abstract

Objective: To evaluate the feasibility of conducting a cohort randomized controlled trial (RCT) of a nurse-led package of care for knee pain and determining a treatment sequence for use in a future trial.

Methods: This study was an open-label, three-arm, single-centre, mixed-methods, feasibility cohort RCT. Adults aged ≥40 years with moderate-to-severe knee pain for ≥3 months were eligible. Participants were randomized into group A (non-pharmacological treatment first), group B (pharmacological treatment first), or group C (usual care). The intervention was delivered over 26 weeks. Outcomes were dropout rate, recruitment rate, intervention fidelity, ability to collect outcome data, and treatment acceptability.

Results: Seventeen participants were randomized and enrolled into each of groups A and B (5.2% recruitment rate), and 174 participants were randomized to group C. The participant characteristics at randomization were comparable across the three arms. Coronavirus disease (COVID-19) paused the study from March–November 2020. Participants enrolled in groups A and B before March 2020 were withdrawn at the restart. Of the 20 participants enrolled after the restart, 18 completed the study (10% dropout). The nurse reported delivering most aspects of the intervention with high fidelity. The participants viewed the package of care as structured, supportive and holistic, they learnt about self-managing knee pain, and they could engage with and follow the non-pharmacological treatment. Most found the non-pharmacological treatment more useful than the pharmacological treatment, preferring to receive it before or alongside analgesia. Many self-report questionnaires were not fully completed.

Conclusion: The nurse-led package of care for knee pain was acceptable, with low dropout, although the cohort RCT design may not be feasible for a definitive trial.

Trial registration: ClinicalTrials.gov, https://clinicaltrials.gov, NCT03670706.

Keywords: feasibility, knee pain, cohort RCT, nurse-led, intervention.

Rheumatology key messages

- Patients engaged and were satisfied with the nurse-led treatment, reporting improved knee pain and function.
- Sequencing non-pharmacological treatment before or alongside pharmacological treatment was preferred by most participants.
- The cohort RCT design may not be feasible, given the poor recruitment and completeness of self-reported outcomes.

Introduction

Pain due to OA is a leading cause of disability in older people [1, 2]. Those unable to self-manage their symptoms are likely to first seek help from their general practitioner (GP), accounting for an estimated 880 000 GP consultations annually,

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with the knee or hip the most commonly affected joints [3]. Multiple international guidelines, including the National Institute for Health and Care Excellence (NICE) guidelines, recommend education, strengthening and aerobic exercise, and weight-loss guidance (where applicable) as core, first-line treatment for all patients with OA [4]. Medical and lifestyle advice, analgesics and referral to physiotherapy and/or weight-loss support are available in the NHS primary care setting; however, non-pharmacological options are frequently underused, with an emphasis on analgesic prescription, including opioids [5–7]. While adequate analgesia may aid exercise adherence [8], this has not been formally tested within a randomized controlled trial (RCT). Patients frequently express reluctance to take oral analgesia or NSAIDs for joint pain [9]. Exercise therapy has similar effects on pain and function compared with oral NSAIDs and paracetamol [10], but primary care physiotherapy treatment sessions are often limited and episodic [11]. Additionally, not all physiotherapists feel they have the knowledge, skills or time to provide effective weight management advice [12]. Group-based rehabilitation for joint pain incorporating NICE guidelines is clinical and cost-effective, but not widely available [13, 14].

Given the rising prevalence of OA [15] and increasing pressure within primary care, it is important to determine whether long-term management can be delivered effectively by other health professionals. Nurse-led interventions to manage other conditions demonstrate equivalent or better outcomes compared with usual care, particularly where lifestyle modifications are important [16–18]. Additional value from nurse-led care may arise from communication styles, long-term continuity of care and a focus on psychosocial context [19].

In phase 1 of this study, we trained nurses to deliver an individualized, non-pharmacological intervention for people with knee pain. This included holistic assessment of the person, individualized education, exercise and weight loss advice utilizing evidence-based behaviour change strategies [20]. We demonstrated the intervention was acceptable to patients and could be delivered with a high degree of fidelity [21, 22]. The aim of this present study, phase 2, was to assess the feasibility of conducting a cohort RCT of the intervention. We also explored whether a future trial should provide pharmacological treatment before or after non-pharmacological treatment.

Methods

Study design

This was an open-label, prospective, three-arm, parallel-group, single-centre, feasibility cohort RCT [20].

Recruitment

Potential participants forming our recruitment cohort (Fig. 1) were community-dwelling adults from the Investigating Musculoskeletal Health and Wellbeing cohort that self-reported knee pain or consulted their GP for it [23]. They were posted an invitation letter asking for their willingness to receive information about future trials, requesting them to complete a questionnaire on knee pain and comorbidities, and asking for their permission to use their questionnaire response data as a comparator in future research studies. Those willing and meeting the eligibility criteria (aged $\geq$40 years, having self-reported knee pain on most days of the previous months for $\geq$3 months, and having self-reported knee pain severity of 4–7 on a 0–10 numeric rating scale [24]) comprised the randomization cohort (Fig. 1).

Participants randomized into the two intervention arms were sent further information about the present study and invited to participate. Those returning a reply slip indicating willingness to participate underwent telephone screening for eligibility. Exclusion criteria included being housebound, care-home residents, comorbidities such as dementia, asthma or lung disease requiring regular daily oral CSs, unstable angina, heart failure, stroke with residual weakness or sensory loss, previous or awaiting knee/hip replacement, etc. [20].

Participants randomized to remain in group C were blind to their randomization and not informed of the present study.

Setting

The setting for this research was an academic research facility in a secondary-care hospital campus.

Randomization and masking

Participants were individually randomized using randomly permuted block sizes of 3 and 6, stratified for unilateral or bilateral knee pain. Randomization codes were generated by the study statistician. Allocations to groups were concealed using serially numbered, opaque, sealed envelopes with carbon copy paper prepared by someone external to the study team. Initially, participants were randomized in a 1:1:1 ratio to groups A, B or C. However, due to low recruitment efficiency into the intervention arms, this was changed to 5:5:1.

Participants, nurses delivering the intervention, and the qualitative interviewer were unblinded to the group allocations. Quantitative outcome assessors were blinded to the sequence of treatment.

COVID-19 impact

The study commenced in November 2019 and was paused from March to November 2020.

Intervention

The intervention [25] was a nurse-led package of care comprising non-pharmacological and pharmacological treatments delivered over 26 weeks [20] (Supplementary Data S1, available at *Rheumatology* online). Participants randomized to group A first received the non-pharmacological treatment for 13 weeks, after which the pharmacological treatment was added. Participants randomized to group B received the same treatment in reverse order. If participants randomized to group A already took analgesia, they received no advice to stop or change this during the first 13 weeks. Treatment visits were face-to-face or remote, depending on participant preference.

Control

Usual NHS care. Where patients seek treatment from their GP, this can include medical and lifestyle advice, analgesics and referral (or self-referral) to physiotherapy and/or weight-loss support.

Feasibility outcomes

1) Dropout rate
2) Recruitment rates
3) Number of treatment visits

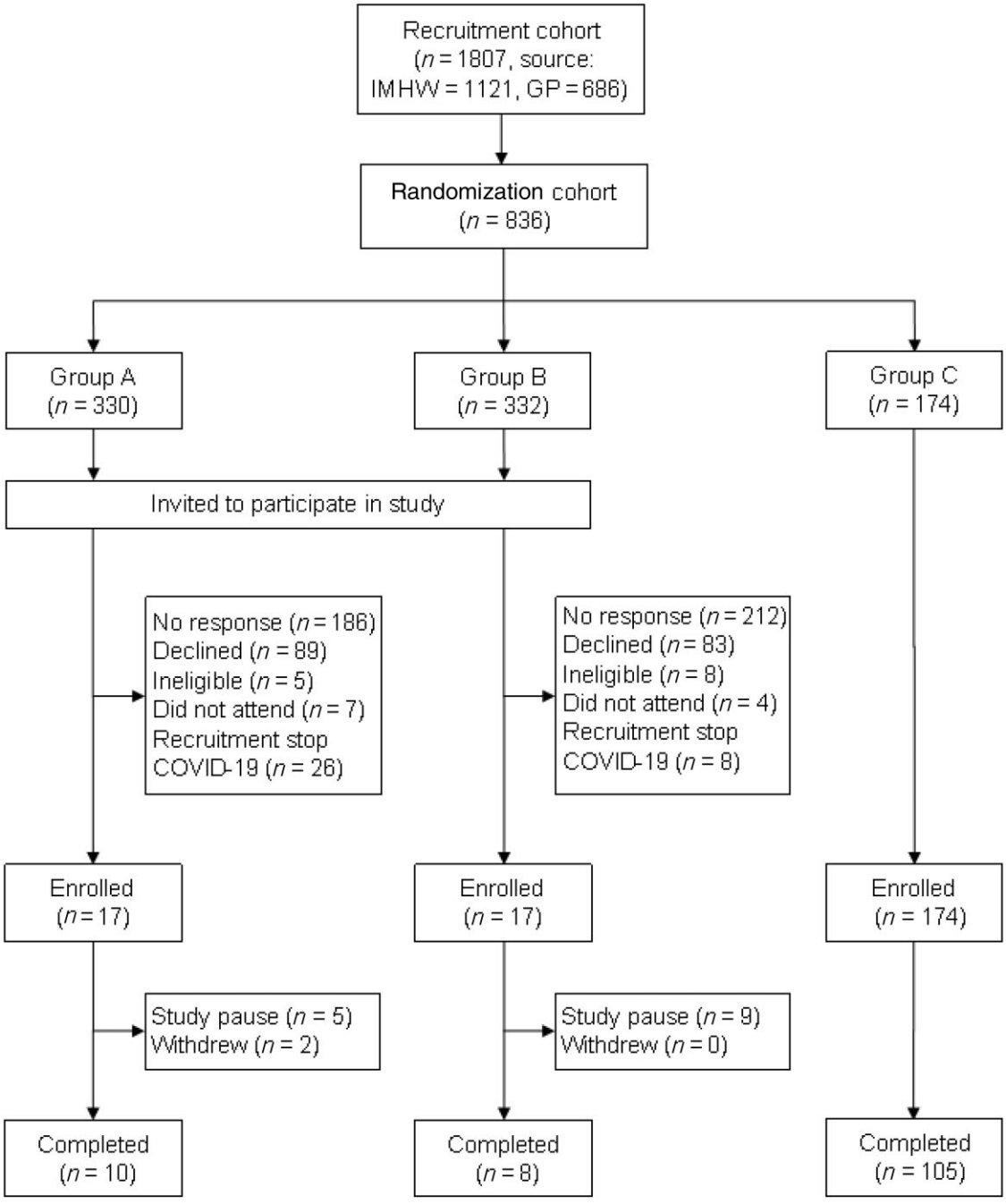

Figure 1. Participant recruitment flow diagram. IMHW, Investigating Musculoskeletal Health and Wellbeing cohort; GP, general practice

4) Completeness of data on WOMAC [24], Short Form (SF-36) v2 [26], EQ5D-5L [27], Hospital Anxiety and Depression Scale (HADS) [28], International Physical Activity Questionnaire (IPAQ) [29], analgesic prescription, Pittsburgh Rehabilitation Participation Scale (PRPS) [30], and Adherence to Exercise Scale for Older Patients (AESOP) [31]
5) Ability to complete the Timed Up and Go Test (TUG) [32], 30-second chair stand test [33], and muscle function testing [34] (groups A and B)
6) Unblinding of quantitative outcome assessor
7) Nurse self-reported fidelity of non-pharmacological and pharmacological treatment delivery
8) (Serious) adverse events [(S)AEs]
9) Nurse views and experience of delivering the treatment (assessed in qualitative interviews)
10) Patient satisfaction with treatment and opinion of treatment sequencing (assessed in qualitative interviews)

Participant research assessments

Questionnaire data and quantitative research assessments for groups A and B were collected at weeks 0, 13 (WOMAC) and 26. Radiographic evaluation was performed at baseline. Questionnaire data was collected from group C by post at weeks 0 and 26.

Participants in groups A and B, and the two research nurses who delivered the intervention were invited to participate in a one-to-one, semi-structured qualitative interview at the end of their involvement with the study. Interviews were digitally audio-recorded, conducted by author A.F. (trained in qualitative research methods) and explored views, acceptability and perceived impact of the intervention and views on treatment sequencing (Supplementary Data S2 and S3, available at *Rheumatology* online).

Sample size

As this was a feasibility study, a formal sample size calculation for between-group comparisons of outcomes was not appropriate. A target sample size of 53 participants per arm (total $n = 159$) was sought to reliably estimate the feasibility outcomes relating to recruitment and retention rates. For the interviews, the target recruitment was up to 20 participants, 10 from each intervention arm.

Data analysis

Quantitative data analysis

Feasibility outcomes were estimated using descriptive statistics. Baseline characteristics were presented using mean (S.D.) and *n* (%). Analgesic use was presented using *n* (%).

For the fidelity assessment, the proportions of the intervention items in the non-pharmacological treatment that were fully, partially or not delivered were calculated. Pharmacological treatment booklets were reviewed to determine whether participants were considered for all drugs to be used in the study.

Completeness of outcome data was assessed by calculating the proportion of questionnaires fully completed.

An exploratory between-group comparison of candidate outcomes (primary outcome: WOMAC pain score) of a future trial was conducted by randomized group at the week 26 follow-up, with emphasis on the point estimates and 95% CIs. Data analyses were performed in STATA 16 [35].

Qualitative data analysis

Data were analysed using inductive thematic analysis [29]. Interviews were transcribed using an automated transcription service. Transcripts were checked for accuracy against the audio-recording by A.F., anonymized and imported into NVivo 12. This step acted as data familiarization. After the first four patient interviews, A.F. and P.A.N. read the transcripts and independently coded segments of text. Discussion of the initial codes and themes resulted in a working analytical framework. Areas to explore further were added to the interview guide. Once all the interviews had been conducted, A.F. applied and refined the analytical framework to the remaining transcripts, which through discussion with the wider team resulted in a final set of themes and subthemes. The nurse interview data mapped onto the themes identified in the patient interviews; hence, these were analysed and are presented together.

Ethical approval

This study complies with the Declaration of Helsinki. It was approved by the East Midlands-Derby REC (18/EM/0288) and was registered with ClinicalTrials.gov (No. NCT03670706). Participants provided their written informed consent before any assessments or interventions were undertaken.

Results

Recruitment and dropouts

Of the 1807 people in the recruitment cohort, 836 were eligible, willing, and randomized into the cohort RCT (Fig. 1). Of those randomized, 17 were enrolled into each intervention arm, and 174 were allocated to group C. The recruitment rate, defined as the number of participants enrolled in groups A and B out of the number randomized, was 5.2%. Participant characteristics at randomization and enrolment (Table 1; Supplementary Table S1, available at *Rheumatology* online) were comparable between the three arms. Most were older, female, and of white ethnicity with two or more comorbidities. Of the 174 participants allocated to group C, 105 (60.3%) returned week 26 questionnaires. Demographic and disease characteristics of those in group C who completed follow-up were comparable with those of participants allocated to group C at baseline.

Upon study pause (March 2020), the 14 participants enrolled in groups A and B were withdrawn. Of the 20

Table 1. Enrolled participant characteristics at baseline, and group C participants returning questionnaires at week 26

	Group A ($n = 17$)	Group B ($n = 17$)	Group C[a] ($n = 174$)	Group C[b] ($n = 105$)
Age (years), mean (S.D.)	63.1 (7.5)	66.3 (10.7)	65.8 (11.1)	67.6 (9.2)
Gender, *n* (%)				
Female	12 (70.6)	14 (82.4)	101 (58.1)	57 (54.3)
Male	5 (29.4)	3 (17.7)	73 (42.0)	48 (45.7)
Ethnicity, *n* (%)				
Caucasian	15 (88.2)	16 (94.1)	163 (93.7)	98 (93.3)
Non-Caucasian	2 (11.8)	1 (5.9)	11 (6.3)	7 (6.7)
BMI, *n* (%)				
<25 kg/m^2	3 (17.7)	7 (41.2)	34 (19.5)	22 (21.0)
25–30 kg/m^2	2 (11.8)	6 (35.3)	63 (36.2)	33 (31.4)
≥ 30 kg/m^2	12 (70.6)	4 (23.5)	77 (44.3)	50 (47.6)
Indices of multiple deprivation tertiles, *n* (%)				
Most deprived	9 (52.9)	7 (41.2)	49 (29.0)	26 (25.0)
Medium	2 (11.8)	6 (35.3)	69 (40.8)	41 (39.4)
Least deprived	6 (35.3)	4 (23.5)	51 (30.2)	37 (35.6)
Smoking history, *n* (%)				
Never smoker	11 (64.7)	12 (70.6)	89 (51.2)	55 (52.4)
Ex-smoker	4 (23.5)	5 (29.4)	71 (40.8)	45 (42.9)
Current smoker	2 (11.8)	0 (0.0)	13 (7.5)	5 (4.8)

(continued)

Table 1. Continued

	Group A ($n = 17$)	Group B ($n = 17$)	Group C[a] ($n = 174$)	Group C[b] ($n = 105$)
Alcohol consumption, *n* (%)				
<3 units per day	12 (70.6)	16 (94.1)	156 (89.7)	95 (90.5)
≥3 units per day	5 (29.4)	0 (0.0)	18 (10.3)	10 (9.5)
Missing	0 (0.0)	1 (5.9)	0 (0.0)	0 (0.0)
Comorbidities[c], *n* (%)				
None	1 (5.9)	2 (11.8)	17 (9.8)	7 (6.7)
One	2 (11.8)	1 (5.9)	41 (23.6)	17 (16.2)
Two or more	14 (82.4)	14 (82.4)	116 (66.7)	81 (77.1)
WOMAC, mean (S.D.)				
Pain score[d]	7.9 (4.8)	7.4 (4.4)	7.8 (4.8)	7.6 (4.6)
Physical function score[e]	31.7 (14.6)	25.3 (12.7)	24.7 (16.6)	23.4 (16.6)
Index score[f]	43.0 (22.0)	37.4 (18.2)	36.5 (23.3)	35.3 (23.3)
Short Form (SF-36), mean (S.D.)				
Physical health score	33.2 (5.2)	33.3 (6.5)	32.8 (6.2)	32.4 (6.0)
Mental health score	41.7 (6.5)	42.2 (4.2)	43.5 (7.2)	44.6 (6.3)
EQ5D-5L, mean (S.D.)				
Index score	0.5 (0.2)	0.6 (0.1)	0.6 (0.3)	0.6 (0.2)
Visual Analogue Scale	66.3 (25.2)	71.6 (17.5)	66.8 (19.9)	66.9 (19.1)
Hospital Anxiety and Depression scale, mean (S.D.)				
Depression score	5.4 (3.6)	5.1 (2.7)		5.8 (4.5)
Anxiety score	6.5 (4.0)	7.2 (5.3)		6.1 (4.8)
MET-min per week, median (IQR)	2193 (990–3510)	3217.5 (2068.5–5981.8)		
MET-min per week, mean (S.D.)	2944.4 (3078.9)	4005.7 (2719.2)		–
Pain score[g], mean (S.D.)	5.8 (1.9)	5.3 (2.2)		–
Analgesic use[h], *n* (%)				
Paracetamol	5 (29.4)	9 (52.9)		–
Oral NSAID	2 (11.8)	8 (47.1)		–
Topical NSAID	1 (5.9)	3 (17.6)		–
Tramadol	0 (0.0)	1 (5.9)		–
Pregabalin	0 (0.0)	0 (0.0)		–
Gabapentin	5 (29.4)	2 (11.8)		–
Co-codamol	7 (41.2)	2 (11.8)		–
Codeine/dihydrocodeine	1 (5.9)	1 (5.9)		–
Morphine sulphf	1 (5.9)	0 (0.0)		–
Blood results, mean (S.D.)				
HbA1c (mmol/mol)	39.1 (5.2)	43.0 (9.6)		–
Cholesterol (mmol/l)	5.1 (1.8)	5.4 (1.4)		–
Triglycerides (mmol/l)	1.5 (1.0)	1.5 (0.7)		–
HDL cholesterol (mmol/)	1.6 (0.3)	1.6 (0.3)		–
LDL cholesterol (mmol/l)	2.4 (0.8)	3.1 (1.3)		–
Cholesterol HDL ratio (mmol/l)	3.3 (1.1)	3.4 (0.9)		–
Non-HDL ratio (mmol/l)	3.5 (1.7)	3.8 (1.3)		–
CRP (mg/l)	5.1 (5.2)	3.7 (2.2)		–
Muscle function[i], median (IQR)				
Peak isometric strength (Nm), median (IQR)	95 (72–138)	97 (84–119.5)		–
Total work output (Nm)	1332 (929–1700)	1211.5 (881–1456.5)		–
Radiographic OA[j], *n* (%)	10 (59)	12 (70.5)		–
Timed Up and Go, mean (S.D.)	11.2 (3.5)	9.1 (2.6)		–
30 s sit-to-stand, mean (S.D.)	11.8 (1.2)	10.2 (2.9)		–

[a] Randomized.
[b] Returned week 26 questionnaire.
[c] Comorbidities included: angina, arthritis, asthma, back/spine problem, cancer, dementia, diabetes, FM, gout, heart attack, heart failure, hypertension, kidney disease, lung disease, OA, osteoporosis, RA or stroke.
[d] The WOMAC pain score ranges from 0 to 20, with high scores equating to greater pain.
[e] The WOMAC physical function score ranges from 0 to 68, with higher scores equating to greater difficulty in moving around and looking after oneself.
[f] The WOMAC index score ranges from 0 to 96, with higher scores equating to worse outcome.
[g] Using a scale of 0–10, where 0 is 'no pain' and 10 is 'pain as bad as could be'.
[h] On the most painful knee.
[i] Participants could report more than one type of analgesia.
[j] Proportion with K&L TFJ or PFJ score ≥2 in at least one knee.
IQR: interquartile range; HDL: high-density lipoprotein; K&L: Kellgren and Lawrence score; LDL: low-density lipoprotein; PFJ: Patellofemoral joint; TFJ: Tibiofemoral joint.

participants recruited after study restart, one in group A withdrew for personal reasons and one could not be contacted. The dropout rate for participants recruited after the study restart was 10% for groups A and B combined, and 39.7% for group C (Fig. 1). If participants recruited before the coronavirus disease (COVID-19) pandemic and withdrawn due to the lockdown are considered, the dropout rate was 47% ($n = 16/34$).

Treatment visits

The 18 participants who attended a week 26 visit underwent a median (interquartile range) of 5 (4–6) face-to-face

treatment visits [Group A: 4 (4–5), Group B: 5.5 (4–6)] and 1 (0–2) remote treatment contact [Group A: 2 (0–2), Group B: 0.5 (0–1)].

Completeness of outcome data

The completeness of the WOMAC pain scores was high at each time point (Table 2), and scores were comparable across all groups (Table 3). The data for other outcome measures at week 26 were comparable across all groups at each time point (Supplementary Tables S2 and S3, available at *Rheumatology* online); however, several questionnaires had high levels of missing data (Table 2).

Ability to complete research assessments

At baseline, all 34 participants in groups A or B performed the TUG test, 26 (76.5%) performed the 30-s sit-to-stand test and 31 (91.2%) performed the muscle function tests. Of the 18 participants who attended a week 26 visit, 17 (94.4%) performed the TUG test, 16 (88.9%) performed the 30-s sit-to-stand test and 13 (72.2%) performed the muscle function tests. There were no instances of unblinding of the quantitative assessors.

Nurse self-reported fidelity of intervention delivery

In the non-pharmacological treatment, the nurse delivered the introduction, assessment, education, and review domains with a high degree of fidelity (Table 4). In the exercise and weight-loss domains, 87.3% and 72% items were fully completed, respectively. In the adjunctive treatment domain, 34.4% items were fully completed.

All participants were considered for paracetamol, topical NSAIDs, and co-codamol (Supplementary Data S4, available at *Rheumatology* online). None of the participants in groups A or B who were not already taking NSAIDs could be considered for it due to contraindications. Analgesic use was comparable at baseline and week 26 (Table 5).

(S)AEs

There was one unrelated SAE (pulmonary embolism), and four participants developed AEs [worsening knee pain ($n = 2$), worsening back pain/sciatica ($n = 2$)].

Intervention views, experience and satisfaction

The 18 participants who completed a week 26 study visit, and one research nurse participated in an interview. Five themes, described below, were generated from the data (illustrative quotes, designated by lower-case letters, Box 1).

A structured, supportive and holistic programme

Overall participants preferred this treatment to usual NHS care, which had left many dissatisfied.[a, b] In particular, they valued its comprehensive approach, and having sufficient focus, time and support for the non-pharmacological treatment to feel comfortable with the advice given.[c] The nurse also felt the treatment length was important for the same reason.[d] The nurse was comfortable delivering the non-pharmacological treatment but needed reassurance from a physiotherapist in the initial stages of prescribing exercises.[e] Participants trusted the nurse's expertise and advice, and valued the nurse's ability to listen to their individual needs, discuss and demonstrate the treatment, and build a therapeutic relationship.[f]

Learning new approaches to self-managing knee pain

Participants' key learning from the treatment were that strengthening muscles around the knee would support it better and reduce pain, and they learnt the specific exercises required to achieve this.[g] Two participants still felt that walking or cycling had similar or greater benefits on their knee pain compared with the prescribed exercise.[h] Some also reported learning that losing weight reduces strain on knees,[i] lessening knee pain, and which dietary changes would support steady weight loss. Almost all demonstrated an understanding that the treatment should be continued long term to avoid progressive worsening of OA.

Engagement with the non-pharmacological treatment and following the provided advice

Most participants were amenable to following the non-pharmacological advice, motivated by the prospect of reduced knee pain and improved knee function and mobility.[j] Facilitators to exercise included having the exercise diary and demonstration sheets as an *aid-mémoire*, nurse follow-up, reinforcement of advice, encouragement to continue, and prescription of simple, achievable exercises that could be incorporated into daily routines and were adjusted or progressed according to individual ability.[k] Barriers to following

Table 2. Completeness of questionnaire outcome data

Questionnaire	Fully completed, *n* (%)		
	Baseline	Week 13	Week 26
WOMAC			
Pain score	740 (89.7)[a]	20 (100)[c]	110 (89.4)[d]
All questions	510 (61.8)[a]	10 (50.0)[c]	70 (56.9)[d]
Hospital Anxiety and Depression Scale	766 (92.9)[a]		35 (28.5)[d]
Short Form (SF-36) v2	630 (76.4)[a]		7 (38.9)[e]
EQ5D-5L	772 (93.6)[a]		15 (83.3)[e]
International Physical Activity Questionnaire	12 (35.3)[b]		5 (27.8)[e]
Analgesic prescription	31 (97.1)[b]		18 (100)[e]
Pittsburgh Rehabilitation Participation Scale (PRPS)			14 (77.8)[e]
Adherence to Exercise Scale for Older Patients			18 (100)[e]

[a] Randomization cohort (total $n = 825$).
[b] Intervention arms only (total $n = 34$).
[c] Intervention arms only (total $n = 20$).
[d] Intervention and control arms (total $n = 123$).
[e] Intervention arms only (total $n = 18$).

Table 3. WOMAC pain scores at weeks 13 and 26

Time-point	Group	*n*	Mean (S.D.) (max. score 20)	Mean difference [95% CI]
Week 13				
	Group A	10	7.20 (4.52)	
	Group B	10	7.60 (4.62)	Group A – Group B = −0.40 [−4.69, 3.89]
Week 26				
	Group A	10	7.10 (5.64)	Group A – Group B = −1.6 [−3.52, 6.72]
	Group B	8	5.50 (4.27)	Group A – Group C = 0.25 [−3.21, 3.71]
	Group C	92	6.85 (5.20)	Group B – Group C = −1.35 [−5.11, 2.41]
	Groups A and B	18	6.39 (5.01)	Groups (A and B) – Group C = −0.46 [−3.10, 2.18]

Table 4. Fidelity of intervention delivery in the non-pharmacological treatment

Domains	Total number of deliverable intervention items[a]	Items fully completed, *n* (%)	Items partially completed, *n* (%)	Items not completed, *n* (%)
Introduction	199	198 (99.5)	0 (0)	1 (0.5)
Assessment	573	569 (99.3)	1 (0.2)	3 (0.5)
Education	574	549 (95.6)	9 (1.6)	16 (2.9)
Exercise	637	556 (87.3)	10 (1.6)	71 (12.8)
Weight loss[b]	364	262 (72.0)	27 (7.4)	75 (28.6)
Adjunctive	253	87 (34.4)	2 (0.8)	164 (64.8)
Review	87	85 (97.7)	2 (2.3)	0 (0.0)

Presented as the proportion of intervention items fully, partially or not delivered within each domain across all non-pharmacological sessions.
[a] The total number of intervention items that the nurse had the opportunity to deliver in each domain (total number of intervention items within each domain across all sessions **minus** the number of items that the nurse determined were not applicable for a patient).
[b] Where applicable.

Table 5. Analgesic use at baseline and week 26 in intervention arm participants completing all study visits[a]

	Baseline			Week 26		
	Group A *n* = 10	Group B *n* = 8	Total *n* = 18	Group A *n* = 10	Group B *n* = 8	Total *n* = 18
Paracetamol, *n* (%)	4 (40)	5 (62.5)	9 (50.0)	4 (40)	6 (75)	10 (55.6)
Topical NSAID, *n* (%)	0 (0)	2 (25)	2 (11.1)	2 (20)	2 (25)	4 (22.2)
Oral NSAID, *n* (%)	2 (20)	5 (62.5)	7 (38.9)	3 (30)	3 (37.5)	6 (33.3)
Tramadol, *n* (%)	0 (0)	1 (12.5)	1 (5.6)	0 (0)	0 (0)	0 (0.0)
Gabapentin, *n* (%)	2 (20)	0 (0)	2 (11.1)	1 (10)	0 (0)	1 (5.6)
Co-codamol, *n* (%)	4 (40)	0 (0)	4 (22.2)	2 (20)	0 (0)	2 (11.1)

[a] The percentages in a column may not add up to 100%, as participants could use any number of different drugs at a time.

prescribed exercise included low motivation, perceiving the exercises as too hard, painful, or boring, or other physical activity taking their time and energy.[(l)]

Facilitators to weight-loss advice included regular food diary feedback[(m)] consisting of small, achievable changes, and provision of written NHS weight loss advice. The nurse also noted the food diaries were a useful talking point with which to engage participants in making changes. Some were motivated to lose weight after a blood test showed they were prediabetic. Barriers to following weight-loss advice included low motivation during the COVID-19 lockdown, believing they did not need to lose weight, and not finding the NHS advice relevant to their dietary needs.[(n)]

Most participants felt confident to continue following the non-pharmacological treatment on their own,[(o)] driven by a notable improvement in knee pain and function, weight loss, and/or wanting to see continued benefit.[(p)] A few decided to only continue their preferred exercises, rather than all the advised exercises.

Usefulness of pharmacological treatment and sequencing preference

Although some found it useful, many reported the pharmacological treatment advice as the least useful treatment aspect. Reasons included perceiving analgesics as unsuitable treatment for[(q)] or having little impact on knee pain, and not having their analgesics escalated (already being on potent analgesics). Many were willing to use topical NSAIDs only.

When asked for preference regarding the order of the treatment, most of group A (non-pharmacological treatment first) and half of group B participants, preferred or would have preferred to receive non-pharmacological treatment first. These participants considered non-pharmacologic treatments more helpful in addressing knee pain, analgesia as unnecessary or something that may affect their adherence to the non-pharmacological treatment due to reduced pain, and/or that the full 26 weeks with the nurse meant they saw the benefits of the prescribed exercises during the treatment period.[(r)] Half of those in group B preferred analgesia first

Box 1. Illustrative quotes

a) *I think it would be absolutely marvellous for that [study intervention to be usual care], rather than just to go in and say, "Oh yeah, you got arthritis, just go away and carry on as you have been doing." Which is what? What point is there in that? What is the point? Makes me angry, actually.* [KPS1206]
b) *I was kind of at a bit of a loss, actually.* [KPS1145]
c) *It's a case of you're not just shoving pills down someone's throat, that you're giving them alternatives and advising about managing the pain and weight loss and things like that, but then giving them the support to see it through.* [KPS1419]
d) *I think that 6 months is excellent time to get to know them and make the change, I think that 6-month period is ideal time for it. You don't want any shorter time than that.* [Nurse]
e) *At first, I was a bit alarmed, as I say. You know, I did go for a bit of reassurance to* [physio trainer] *… getting them to do an exercise and thinking 'Should I be allowing them to do this or not?' But I think after a few of them and having some reassurance, I was fine with it.* [Nurse]
f) *From the nurse it was more in depth, 'cause they seem to have a lot more time to offer you and it was explained really well. I know when you go to the physio you're given a sheet to do the exercises, but I was actually shown what was expected of me. That helped. And like I say, because you're followed up and they're there for you. Yeah, it's a lot better.* [KPS1082]
g) *Yeah, like things can be improved by exercise rather than, I thought walking that I did was good exercise in itself, but that you need to exercise specific areas.* [KPS1081]
h) *Some of the pushing, you know, exercises I can do better, or more enjoyably when I'm riding my bike. I didn't see much value in housebound exercises.* [KPS1203]
i) *You learn more about what you can do, what strengthens your knee, for instance, and you know. like I know. I've got to lose weight. I know that weight's a problem.* [KPS1286]
j) *I suppose for me if I can make some changes, that hopefully as I get older things are going to be easier for me. You know, that I'm more mobile. And I would try it. I'd do it and I think it's important.* [KPS1267]
k) *Well, they started comfortably, not over stretching … There was one I couldn't do because it, cause I've got heart problems as well, and that affected how my heart was working. And she tweaked that so I could do it, so that was brilliant.* [KPS1082]
l) *Once the gardening thing started, for example, that takes 3 hours on a Wednesday morning … so I can't say I rush back on a Wednesday afternoon to do, you know, some of the exercises. Obviously if I've done that on the morning that's my lot for the day sort of thing.* [KPS1176]
m) *I think coming back to the, to see* [nurse] *and somebody actually looking at your diary, what you were eating. Having confirmation because somebody is looking at it that you are on the right track … emphasizing foods that perhaps you ought to avoid or reduce.* [KPS1142]
n) *All that we've got is the NHS diet plan, and I must admit it wasn't greeted very well by participants. They found it restricting, out of date, not what they would want to do. And there are so many other diets out there now.* [Nurse]
o) *It's given me the confidence to carry on with things that I need to do at home.* [KPS1200]
p) *I'm going to carry on with the exercise because they have done a big benefit.* [KPS1504]
q) *To me injections and any pain relief is just masking what's wrong with you. It's not sorting out the problem is it?* [KPS1081]
r) *The fact that I've had 6 months to do the exercises instead of 3 has meant that I've noticed the benefits more, so for me it worked better the way it did, the exercise/food management part first.* [KPS1200]
s) *At the same time. Yeah, I think so. Because then you're controlling it better I would think … first off, you're just using this gel for like a week or two, and you think 'oh, like heaven' and then you know, then the exercise and everything.* [KPS1555]
t) *There wasn't anyone that I saw that when I delivered the pain side, so the pharma side first, there wasn't any of those that I wouldn't have done the diet and exercise as well as.* [Nurse]
u) *I did get to the top of the stairs just standing upright and holding the rail. I can't tell you how overjoyed I was by that. I can't emphasise that enough, how when I suddenly thought 'hang on a minute, I couldn't do that this time last year.'* [KPS1206]
v) *I think when you've not got, had the pain afterwards, it gives you more confidence then to use your knees. So it's giving me more confidence in them.* [KPS1142]
w) *Very effective! For those people who did it. Well, as I say, I was quite surprised at how effective it can be for them and how positive it made them at the end of the day.* [Nurse]
x) *I don't feel I need a knee replacement while ever I'm carrying on as I am doing* [KPS1176]; *in a way, it's given me hope of doing normal things again.* [KPS1504]
y) *I'm feeling more positive that I'm in control. Yeah, and I can do something about it personally* [KPS1142]
z) *I think it's helped my knee to some extent. But I think it's that far gone that if I did the exercises for the last 5 years everyday it wouldn't have stopped it being needed to be operated on.* [KPS1081]

but would have liked the exercise to start sooner.[s] The nurse was confident that all participants would have been capable of starting non-pharmacological treatment straightaway.[t]

Impact of knee pain on daily life before and after the package of care

Most participants reported an improvement in their knee pain and stability by week 26. This meant they could resume usual daily activities, e.g. walking up and down stairs, with their pain greatly reduced[u] and improved mobility, which gave them confidence in using their knees.[v] Some began other forms of exercise. Many reported an improvement in their overall health and well-being, also observed by the nurse, who said the treatment prompted some to invest further in their health. The impact of following the treatment exceeded both the nurse's and participants' expectations.[w] As a result, many participants were optimistic about their knee pain and mobility in the future,[x] having been given individualized tools to self-manage it.[y] A few still expected their knee pain to worsen, and that knee replacement surgery was inevitable. This included those who reported not following the exercise programme fully, or who considered their knee too severely damaged.[z]

Discussion

We tested the feasibility of a cohort RCT of a nurse-led package of care for knee pain. There was a low dropout rate in intervention groups, good fidelity of intervention delivery, and adequate blinding of the quantitative outcome assessor, and it was possible to collect complete outcome data for the primary candidate outcome variable. Participants accepted the intervention, were positive about its delivery by a nurse, and generally preferred to receive non-pharmacological treatment before pharmacologic treatment, or else simultaneously. There was a low recruitment rate into the intervention arms, with only 5% of people approached being willing to take part in the intervention and recruitment challenges predating the COVID-19 pandemic. This suggests that a large number of GP surgeries would be needed to recruit enough participants.

There was high fidelity of delivery of the package of care for most domains of the intervention, except for advice on adjunctive therapies. This was an area of low fidelity in phase 1 that has not improved, despite reinforcement training [21], suggesting this aspect should be delivered by other health professionals with relevant expertise, e.g. an occupational therapist or orthotist.

The qualitative results align with other studies demonstrating that lifestyle interventions delivered by a nurse are feasible, delivered with good fidelity and participant retention, and acceptable to patients [16, 36–39]. Similar to a study aiming to improve patient engagement with gout treatment, participants in this study preferred treatment delivered by a nurse [40], had improved understanding of their condition, had engagement with its long-term management and were motivated to continue following treatment after experiencing positive impacts [37]. In line with a systematic review of nurse-led lifestyle interventions, patient acceptance of treatment was driven by the nurse's ability to build a therapeutic relationship, provide individualized care, motivate patients to meet their treatment goals, and provide frequent follow-up [38]. That most participants preferred or would have preferred to receive the nurse-supported exercise programme for 26 weeks indicates the importance of prolonged support and regular follow-up to optimize engagement in non-pharmacological treatment for knee pain.

Except for the WOMAC pain score, many self-reported outcome measures were not completed well. The muscle function test could not be completed by four participants at week 26 due to pain while undertaking the test. Data collection should be optimized to reduce participant burden in future studies with this population, by administering fewer self-report questionnaires and a limited muscle function protocol.

Strengths of this study include community cohort recruitment, high treatment fidelity and a low dropout rate. The cohort RCT design made the consent procedure similar to that of standard health care, in which participants are asked to consent to treatments they are being offered and not informed about treatments they cannot access [41]. This minimizes non-participation of people with a strong preference for receiving the trial interventions [42, 43], and reduces risk of withdrawal or biased outcome reporting that may be caused by knowledge of not being allocated to the preferred arm [44].

A key limitation of this study is the low recruitment rate into the intervention arms, which was lower than studies recruiting from similar cohorts [45, 46]. This precluded observing any signal of efficacy, although a definitive trial can provide robust estimates of effectiveness. We did not explore why people were willing to join the recruitment cohort but declined or did not respond to the invitation to take part in the intervention. We also did not record what treatment those in usual care received. Intervention delivery in an academic research centre located on a secondary-care hospital campus may have led to greater improvements due to expectation bias. There was a two-step eligibility assessment applied to participants in the intervention arms; however, those enrolled in the intervention arms had comparable disease and demographic characteristics to those of participants in usual care.

In summary, a future trial of the nurse-led package of care for knee pain appears feasible, as there was a low dropout rate, and patient acceptability and engagement in self-managing knee pain. To determine the validity of a nurse-led intervention, future trials should compare it to physician-led care in which the physician has easy access to therapy services. The feasibility of using a cohort RCT design could not be proven. Future trials may benefit by recruiting from patients seeking treatment for knee pain.

Supplementary material

Supplementary material is available at *Rheumatology* online.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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