PHYSIOHTERAPY REVIEW (PREVIOUSLY MEDYCYNA MANUALNA)

TITLE PAGE

Title: Factors associated with trial recruitment and retention of people with osteoarthritis: analysis of 215 randomised controlled trials from 2013-2021.

Running Header: Recruitment and retention in osteoarthritis trials

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DECLARATIONS

Contributorship: The study was designed by TS. Data collection was carried out by SW and CYDW. Data analysis was carried out by TS, SW and CYDW. The first draft of the manuscript was prepared by SW, CYDW and TS. All authors contributed to revisions of the manuscript and approved the submitted version. Guarantor TS.

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ABSTRACT

AIMS: To identify recruitment and retentions rate in randomised controlled trials (RCTs) recruiting people with hip or knee OA, and to determine factors which affect these.

MATERIALS & METHODS: Pubmed search identified RCTs published between 2013-2021, recruited people with hip or knee OA. Regression analyses determined participant and trial factors which may have affected recruitment or retention rates.

RESULTS: 215 RCTs were included. Mean recruitment rate was 63.2%. Mean follow-up rate was 88.4%. Trials had higher recruitment rates if publicly-funded (Odd Ratio (OR): 1.47; 95% Confidence Intervals (CI: 1.12, 1.92), did not recruited people with medical comorbidities (OR: 0.55; 95% CI: 0.41, 0.73), offered a drug intervention as their experimental intervention (OR: 0.50; 95% CI: 0.29, 0.88), recruited from hospitals (OR: 1.42; 95% CI: 1.07, 1.80) and had shorter follow-up durations (OR: 0.95; 95% CI: 0.91, 0.99). Trials had higher retention rates if their experimental group had lower baseline pain scores (OR: 1.20; 95% CI: 1.02, 1.41), control group had higher pain scores (OR: 0.84; 95% CI: 0.72, 0.99), recruited from fewer sites (OR: 0.98; 95% CI: 0.96, 0.99), with shorter follow-up durations (OR: 0.96; 95% CI: 0.92, 0.99).

CONCLUSION: Factors which impact on recruitment and retention rates in OA RCTs include: funding source, baseline pain levels, comorbidity status, location and number of recruitment sites and follow-up duration. These factors should be considered when conducting future OA RCTs.

Keywords: RCT; design efficiency; recruit; follow-up; attrition; arthritis

INTRODUCTION

Randomised controlled trials (RCT) remain the gold-standard research methodology to investigate interventions. Patient recruitment remains a key element for the successful conduct of clinical trials.[1] However recruitment inefficiencies such as screening non-eligible participants and low conversion of screening to consent through missing eligible participants frequently occur, threatening the timely completion of trials. Duley et al's[2] survey among the UK Clinical Research Collaboration (UKCRC) registered Clinical Trials Units reported that recruitment inefficiency was the key reason why recruitment targets were not met. Similarly, Huang et al[1] reported that 86% of RCTs failed to recruit to their target number of participants within the planned timeframe, with 19% terminated early due to insufficient recruitment.[1] This challenge in recruitment and retention of trial participants jeopardizes the completion of important clinical research, whilst also being inefficient in relation to time and resources for funders, trialists, clinicians and patients.[3,4] Thus this is considered a research 'waste'.[5,6]

Musculoskeletal conditions are the second largest cause of disability.[7] There are 1.71 billion people suffering from musculoskeletal conditions globally.[8] The global prevalence of knee osteoarthritis is 3.8% and hip osteoarthritis is 0.9%.[9] Incidence of osteoarthritis increases with age, increasing by approximately three percent annually.[10,11] There are multiple treatment options to reduce symptoms including pharmacological, non-pharmacological, surgical and alternative interventions.[12] Trials are paramount to inform the offer of evidence-based interventions to this growing population.

Recruitment rates in osteoarthritis clinical trials are relatively poor.[5,6] Trials frequently do not meet recruitment targets.[5,6] Approximately 85% of clinical trials in do not reach their recruitment targets within the planned timescale[1] with 19% terminating before the target sample size is reached.[13] Similarly, retention has more recently been highlighted as an important threat to the successful completion and validation of clinical trials.[14,15] High attrition (greater than 20%)[16] and not recruiting the pre-specified sample size for statistical power result in inefficient trial designs, delaying or preventing the answering of original clinical questions with sufficient power and precision.

AIMS

There is uncertainty to what factors affect recruitment rates and retention rates and their efficiency in osteoarthritis trials. The aim of this study is to identify the recruitment and retention rates in osteoarthritis RCTs published from 2013-2021 and to explore possible factors which affect these. This is important as the findings of this analysis will provide insights into strategies which may improve recruitment, and therefore inform more successful, future recruitment and retention strategies for clinical trials of individuals with osteoarthritis.

MATERIALS AND METHODS

We undertook a bibliometric analysis to assess factors which influence recruitment and retention to osteoarthritis trials. Studies published between January 2013 to January 2021 were identified through a PubMed search. The search strategy is presented in **Supplementary Table 1**. Studies were included if they were: RCTs recruiting people with hip and/or knee osteoarthritis; presented as full-text publications. We excluded studies if they were: publications which reported a protocol; participants who were recruited after total hip/knee arthroplasty; secondary data analyses of previous RCTs; and publications which were not published in English as full-text papers. Studies were identified by two reviewers (SW/CYDW); who independently screened all titles and abstracts from the search results. The two reviewers independently screened all potentially eligible studies at full-text level. Only studies which met the eligibility criteria, as agreed by the two reviewers, were included. Disagreement on study eligibility were resolved through discussion, adjudicated by a third reviewer (TS).

Data were extracted from each included paper by one reviewer (CYDW/SW) and then verified by the second (SW/CYDW). Data extracted included: number of participants; location of osteoarthritis; sample size; country of origin; source of funding; number of participants screened; number of participants assessed at last assessment; participant educational status; ethnicity; age; gender; pain score; number of participants with comorbidities; number of participants with single/multi-joint osteoarthritis; location of recruitment; intervention type (control and experimental); number of sites; whether the sample size calculation was met; and duration of follow-up. Where disagreement occurred in data extraction, these were resolved through discussion, adjudicated by a third reviewer (TS).

Data Analysis

An assessment of data normality was performed using the Kolmogorov–Smirnov test. Data were descriptively analysed using mean and standard deviation (SD) values for continuous data and frequency and percentages for categorical data. Randomisation rate was expressed as the number of participants randomised as a percentage of the total number of participants screened for eligibility. The follow-up rate was expressed as the number of participants that failed to complete the trial as a percentage of the number randomised. Subgroup analyses were conducted using regression analyses where arbitrary cut-points of recruitment rates of 80% and above were compared to recruitment rates of less than 80% and follow-up rates of 90% and above were compared to those of less than 90%. This was performed to understand the potential trial characteristics and demographic features related to randomisation rate and follow-up rate. Bonferroni corrections were applied to all analyses to account for the risk of multiple comparison testing. Data for all regression analyses were presented as odd ratio (OR) and 95% confidence intervals (CI). Variables were regarded as having a significant relationship where the p-value was <0.05. All statistical analyses were undertaken on STATA version 16.0 (Stata Corp, Texas, USA).

RESULTS

Participant and Study Characteristics

The results of the search strategy are presented in **Figure 1**. In total, 215 trials were identified and included in the analysis. The characteristics of the recruited participants and 215 trials are presented in **Table 1**. Assessed trials included 91,999 participants who were screened and 36,806 participants who were recruited. In total, 31,691 were assessed at their last assessment. The mean recruitment rate was 63.2% (SD: 29.1). The mean follow-up rate was 88.4% (SD:13).

Recruitment rate

Seven factors were identified as significantly associated with recruitment rate (**Table 2**). All other factors examined were not statistically significant. Studies which were funded by commercial sources (OR: 1.47; 95% CI%: 1.12, 1.92; p=0.005) or recruit people with medical comorbidities (OR: 0.55; 95% CI: 0.41, 0.73; p<0.001) were less likely to have a recruitment rate of 80% or above. Trials which had a longer duration of follow-up were less likely to have recruited 80% or more of the participants they screened (OR: 0.95; 95% CI: 0.91, 0.99; p=0.025).

Trials which recruited from hospitals were more likely to have a recruitment rate above 80% compared to those recruited from community sources (OR: 1.42; 95% CI: 1.07, 1.80; p=0.016). Trials which offered a pharmacological intervention as their experimental intervention were more likely to recruit 80% or more of their screened participants (OR: 0.50; 95% CI: 0.29, 0.88; p=0.017). Whilst there were statistically significant associations between number of site (p=0.009) and whether trials met their sample size calculations (p=0.028), there was minimal difference in the actual numbers who recruited 80% or more of their screened participants (**Table 2**).

Follow-up rate

Four factors were identified as significantly associated with a follow-up rate of 90% or more (**Table 3**). All other factors examined were not statistically significant. Trials where the experimental group presented with lower pain scores were more likely to demonstrate a follow-up of 90% or more (OR: 1.20; 95% CI: 1.02, 1.41; p=0.031). Conversely follow-up rates of 90% or more were demonstrated where control participants had higher pain scores (OR: 0.84; 95% CI: 0.72, 0.99; p=0.037). Trials which recruited a lower number of sites (OR: 0.98; 95% CI: 0.96, 0.99; p=0.026) and where the duration of follow-up was shorter (OR: 0.96; 95% CI: 0.92, 0.99; p=0.015) reported higher follow-up rates of 90% and over, compared to trials with a higher number of sites and longer duration of follow-up (**Table 3**).

DISCUSSION

The findings of this analysis indicate that conversion of screened to randomisation in trials of people with hip and/or knee osteoarthritis was moderately high (mean: 63%) and equally high follow-up rates (88%) at a mean of eight months. Trials were more likely to have higher recruitment rates if they were publicly-funded, did not recruit people with medical comorbidities, offered a pharmacological intervention as their experimental intervention, recruited from hospitals and had shorter follow-up durations. Trials were more likely to have higher follow-up rates if their experimental group presented with lower pain scores at baseline, but control participants had higher scores, recruited from fewer sites and had a shorter duration of follow-up. These findings provide useful insights to aid the design of clinical trials of people with osteoarthritis, to develop more efficient trials.

People with osteoarthritis frequently present with various medical comorbidities.[17] They are approximately three times more likely to have multiple comorbidities compared to people without osteoarthritis.[18] Medical comorbidities in this population commonly include hypertension, heart

diseases and diabetes.[18] The findings of this analysis indicate that recruitment rate was lower in trials which recruited people with medical comorbidities. Given the high proportion of this population who have medical morbidities, excluding people from trials for this reason poses issues regarding external validity.[18] However the results may be, in-part, explained to the hypothesis that people with other morbidities may decline participation due to other time commitments in managing comorbidities,[19] differing views on health priorities over osteoarthritis compared to other comorbidities,[20] or selection bias against people with medical comorbidities. Whilst beneficial for recruitment rates, the compromise made on generalizability by excluding people with comorbidities does not justify this exclusion criterion.

There was a difference in recruitment and follow-up rates dependent on the type of interventions under investigation. Trials investigating pharmacological interventions as their experimental treatment were more likely to recruit over 80% of those screened. This may be related in-part, to an individual's willingness to participate in a drug trial which may be less time-burdensome in intervention participation compared to a rehabilitation trial. It contrasts with the notion that individuals may associate drug trials to a threat of adverse events.[21,22] Nonetheless, the findings suggest that specific attention may be required to improve recruitment rates for non-drug trials for people with osteoarthritis, particularly given that rehabilitation is regarded as a core intervention for this population.[23]

Trials with follow-up rates of 90% or above reported that their experimental group participants had lower pain scores and their control group had higher pain scores. Accordingly, there was higher attrition where participants in the experimental group had higher pain scores pre-operative and the control group had lower scores. Attitudes towards treatment allocation, and perceived intervention effect, particularly for unblinded trials, may have determined whether people continued to follow-up. Previous literature has suggested that people with osteoarthritis have lower compliance to prescribed treatments compared to populations with other long-term conditions such as heart-disease.[20,24] This viewpoint to the disease may be one reason for attrition depending on symptom-levels. Measures to support continued engagement in osteoarthritis trials is therefore particularly pertinent for participants based on their baseline symptoms.

Publicly-funded trials were more likely to have a recruitment rate of 80% or above compared to commercially-funded. The majority of previous evidence on recruitment and retention factors has focused on publicly-funded trials.[25,26] These have reported average retention rates of 89% and

recruitment rates of 0.92 participants per center per month.[25] This study, albeit focusing on trials of osteoarthritis, has explored both commercial and publicly-funded trials, indicating a difference. This may be attributed to participant's attitudes towards commercially-funded trials, potentially demonstrating reduced willingness to participate through less altruistic motivations or suspicious of financial gain for the commercial partner.[27] Alternatively, this may reflect a difference in the site infrastructure and personnel in delivering commercially over publicly-funded trials.[28] There remains uncertainty over what may be the prevailing factor. Nonetheless the results indicate that different support may be made to how commercial trials are communicated and delivered to participants to mitigate this difference in recruitment rates.

Whilst this trial has identified several factors associated with recruitment and retention, it was not the intention to explore strategies which may improve these. Several Cochrane reviews have identified approaches such as telephone reminders, open (unblinded) trial designs, financial incentives and online data collection as potential factors which may be used.[29-31] Consideration of these potential approaches may be made, to address some of the threats identified in this study to recruitment and retention.

Strengths and Limitations

A strength of this study is that it is the only analysis to investigate whether certain variables influence recruitment and retention in musculoskeletal trials. However there are several important limitations. Firstly, we only included English-language publications. Consequently nine papers being excluded. Secondly, we only search Pubmed as the literature database. This was justified as this was anticipated to provide an appropriate source of published RCTs. However it is acknowledged that this is therefore not a systematic review which may have provided a more comprehensive analysis of the evidence-base. Thirdly, data were not consistently reported in each paper. Some papers reported a small number of variables whilst others presented a greater range. Resultantly, for some variables, there were limited data. For example, comorbidities were not universally presented in the same format. It was therefore not possible to determine whether specific comorbidities influenced recruitment or retention. Finally, RCTs which recruited people after surgery were excluded. This was justified as people who underwent surgery had resolved osteoarthritis symptoms. However, surgery is one of the key treatments for osteoarthritis, and therefore is worth further investigation.

CONCLUSIONS

Recruitment and follow-up rates for trials of people with hip or knee osteoarthritis are moderately high. Trials are more likely to have higher recruitment rates if they are publicly funded, do not recruit people with medical comorbidities, offer a pharmacological intervention as their experimental intervention, recruit from hospitals and have shorter follow-up durations. Trials are more likely to have high follow-up rates if their experimental group presented with lower pain scores at baseline, but control participants had higher scores, recruit from fewer sites and have a shorter duration of follow-up. These findings can inform the design of more robust recruitment and retention strategies for future osteoarthritis trials. This will aid the efficiency of trial conduct, thereby reducing research waste, to generate a more timely and robust answer to these important research questions for people with joint pain.

FIGURE AND TABLE LEGENDS

Figure 1: Study flow chart

Table 1: Demographic characteristics

Table 2: Regression analysis on study characteristic factors related to recruitment rate

Table 3: Regression analysis on study characteristic factors related to follow-up rate

Supplementary Table 1: Pubmed search strategy

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Figure 1: Study flow chart

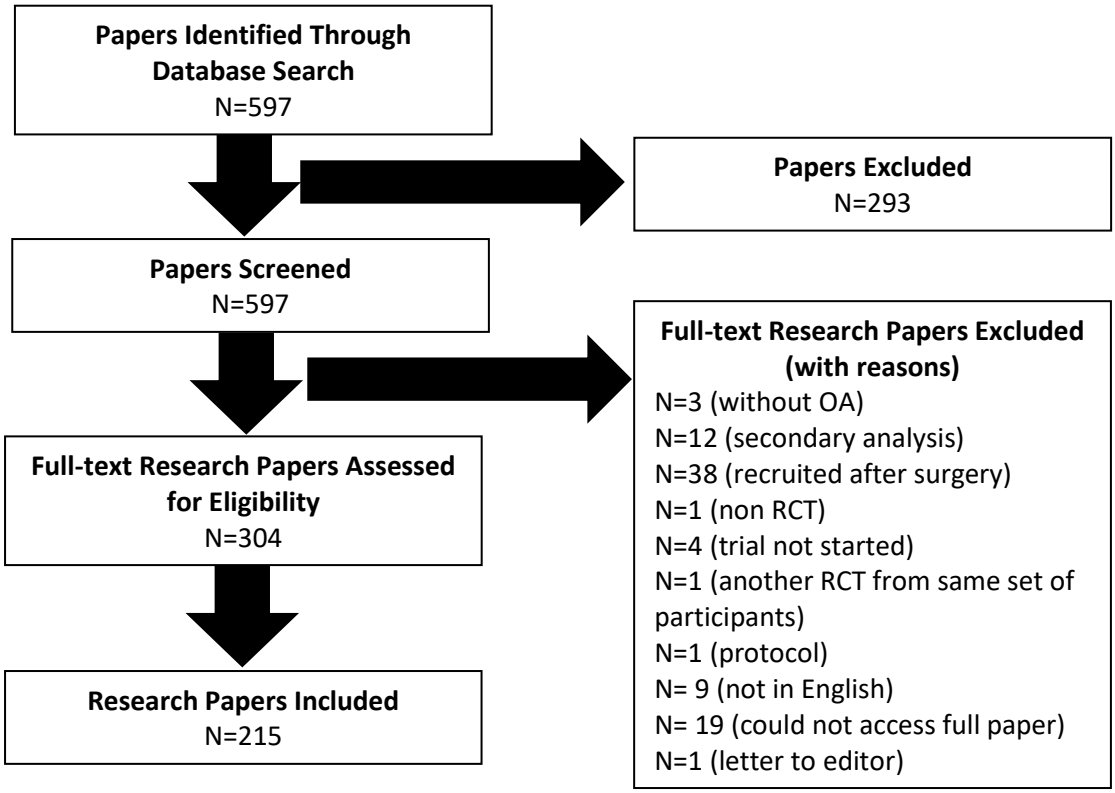

Table 1: Demographic characteristics

		Participants (%)	Number studies
N (studies)		215 (100)	215
N (participants)		163.4 (186.7)	215
Total number participants		36,806	215
Location of OA	Hip	1672 (4.5)	12 (5.6)
	Knee	30,235 (82.1)	188 (87.4)
	Hip and Knee	4899 (13.3)	15 (7.0)
Mean sample size (SD)		163.4 (186.7)	215 (100)
Country of origin	USA	6991 (19.0)	29 (13.5)
	Argentina	113 (0.3)	1 (0.5)
	Australia	4315 (11.7)	22 (10.2)
	Multinational	6995 (19.0)	10 (4.7)
	Brazil	1221 (3.3)	17 (8.0)
	Canada	1960 (5.3)	9 (4.2)
	Chile	29 (0.1)	1 (0.5)
	China	2351 (6.4)	11 (5.1)
	Denmark	771 (2.1)	7 (3.3)
	UK	1602 (4.4)	11 (5.1)
	Finland	174 (0.5)	2 (1.0)
	France	758 (2.1)	3 (1.4)
	Germany	706 (1.9)	3 (1.4)
	Hong Kong	278 (0.8)	2 (1.0)
	India	381 (1.0)	6 (2.8)
	Indonesia	147 (0.4)	1 (0.5)
	Iran	1760 (4.8)	22 (10.2)
	Italy	837 (2.3)	10 (4.7)
	Japan	756 (2.1)	3 (1.4)
	South Korea	569 (1.5)	5 (2.3)
	Lithuania	56 (0.2)	1 (0.5)
	Mexico	56 (0.2)	2 (1.0)
	Morocco	100 (0.3)	1 (0.5)
	Netherland	422 (1.1)	4 (1.9)
	New Zealand	323 (0.9)	3 (1.4)
	Norway	631 (1.7)	4 (1.9)
	Portugal	40 (0.1)	1 (0.5)
	Saudi Arabia	58 (0.2)	1 (0.5)
	South Africa	74 (0.2)	1 (0.5)
	Spain	626 (1.7)	8 (3.7)
	Sweden	69 (0.2)	1 (0.5)
	Switzerland	295 (0.8)	2 (1.0)
	Thailand	497 (1.4)	5 (2.3)
	Turkey	241 (0.7)	4 (1.9)
	Unclear	604 (1.6)	2 (1.0)
Source of funding	non-commercial	13,923 (37.8)	40 (18.6)
	commercial	16,730 (45.5)	109 (50.7)
	none	929 (2.5)	13 (6.0)
	unclear	5049 (13.7)	52 (24.2)

	Commercial and non-commercial	175 (0.5)	1 (0.5)
Number of patients screened (mean; SD)		91,999 (436.0;690.3)	211
Number of patients randomised (mean; SD)		36,806 (171.2;206.2)	215
Number of patients assessed at last assessment (mean; SD)		31,691 (147.4;170.7)	215
Randomisation rate (mean; SD)		63.2 (29.1)	215
Follow-up rate (mean; SD)		88.4 (13.0)	215
Education status	< High School	2127 (5.8)	29 (13.5)
	> College/University	2040 (5.5)	25 (11.6)
	No education	111 (0.3)	7 (3.3)
	Not stated	32,528 (88.4)	200 (93.0)
	Unclear	155 (0.4)	3 (1.4)
Ethnicity	White/Caucasian	7622 (20.7)	31 (14.4)
	Black/African American	1039 (2.8)	21 (9.8)
	Asian	464 (1.3)	18 (8.4)
	Hispanic	35 (0.1)	7 (3.6)
	Pacific Island	64 (0.2)	1 (0.5)
	Multiple Ethnicity	37 (0.1)	5 (2.3)
	Not stated	26,014 (70.7)	190 (88.4)
	Unclear	1199 (3.3)	11 (5.1)
	Other	332 (0.9)	10 (4.7)
Age (mean; SD)	Experimental	61.4 (5.5)	194 (90.2)
	Control	61.8 (4.8)	193 (89.8)
Gender	Male	13,773 (38.1)	197 (91.6)
	Female	22,343 (61.9)	210 (97.7)
Pain: VAS	Experimental	33.8 (47.3)	93
	Control	29.4 (26.3)	92
Pain: KOOS-HOOS	Experimental	55.2 (12.5)	16
	Control	53.3 (14.0)	18
Pain: WOMAC	Experimental	34.0 (61.9)	65
	Control	34.4 (62.2)	65
Pain: NRS	Experimental	25.6 (27.6)	38
	Control	25.8 (32.9)	38
Number of people with comorbidities		1147 (3.1)	8
Multiple or single joint OA	Single	169 (79.0)	170
	Multiple	41 (19.1)	44
	Unsure	4 (1.9)	1
Location of recruitment	Community	125 (58.4)	126
	Hospital	52 (24.3)	52
	Both	17 (7.9)	17
	Not state	20 (9.4)	20
Intervention (experimental) type	Pharmacological	111 (51.8)	112
	Rehabilitation	101 (47.2)	101
	Both	1 (0.5)	1
	Unsure	1 (0.5)	1
Intervention (control) type	Sham	98 (45.8)	99
	Active Intervention	115 (53.7)	115
	Both	1 (0.5)	1

Number of sites	Single site	95 (44.4)	95
	Multiple site	102 (47.7)	103
	Unsure	17 (7.9)	17
Sample size calculation met	Yes	118 (55.1)	118
	No	38 (17.8)	38
	Unsure	58 (27.1)	58
Number of recruitment sites (mean; SD)		10.1 (31.5)	164
Duration of follow-up (mean; SD)		7.5 (8.9)	211

N – number of participants; NRS – numerical rating score; OA – osteoarthritis; SD – standard deviation; UK – United Kingdom; USA – United States of America; VAS – visual analogue scale

Table 2: Regression analysis on study characteristic factors related to recruitment rate

		Recruitment Rate		Odd Ratio (95% CI)	P-Value
		<80% (N=142)	80%> (N=73)		
Location of OA	Hip	122 (85.9)	66 (90.4)	0.85 (0.49, 1.46)	0.055
	Knee	10 (7.0)	2 (2.7)		
	Hip and Knee	10 (7.0)	5 (6.9)		
Source of funding	Non-commercial	26 (18.3)	14 (19.2)	1.47 (1.12, 1.92)	0.005
	Commercial	84 (59.2)	25 (34.3)		
	None	7 (4.9)	6 (8.2)		
	Unclear	24 (16.9)	28 (36.4)		
	Commercial and non-commercial	1 (0.7)	0 (0.0)		
Education status	<High School	12.9 (42.6)	4.1 (15.1)	0.99 (0.97,1.01)	0.253
	>College/University	12.4 (48.1)	3.9 (22.7)	0.99 (0.98, 1.01)	0.608
	No education	0.5 (3.1)	0.6 (3.9)	1.01 (0.93, 1.10)	0.761
Ethnicity	White/Caucasian	48.2 (50.5)	10.7 (56.8)	0.99 (0.99, 1.00)	0.050
	Black/African American	5.3 (24.1)	4.7 (24.7)	1.01 (0.99, 1.02)	0.529
	Asian	1.2 (9.2)	4.0 (28.4)	1.03 (0.98, 1.09)	0.323
	Hispanic	0.2 (1.2)	0.2 (0.9)	1.00 (0.725, 1.39)	0.979
Age	Experimental	61.4 (5.0)	61.2 (6.6)	0.96 (0.83, 1.10)	0.566
	Control	61.6 (5.0)	62.2 (4.7)	1.07 (0.92, 1.23)	0.391
Gender	Male	66.2 (79.1)	64.4 (85.4)	0.99 (0.99, 1.00)	0.500
	Female	103.1 (126.6)	113.1 (168.6)	1.00 (0.99, 1.00)	0.411
Pain: VAS	Experimental	35.9 (57.3)	30.7 (27.6)	1.10 (0.98, 1.24)	0.104
	Control	29.8 (26.5)	29.0 (26.3)	0.91 (0.81, 1.02)	0.110
Pain: KOOS-HOOS	Experimental	50.1 (18.2)	65.9 (9.8)	1.62 (0.82, 3.20)	0.163
	Control	49.2 (18.9)	61.5 (6.3)	0.71 (0.41, 1.23)	0.223
Pain: WOMAC	Experimental	38.3 (68.5)	17.9 (26.8)	0.92 (0.67, 1.27)	0.609
	Control	38.6 (68.7)	18.3 (28.9)	1.07 (0.79, 1.45)	0.667
Pain: NRS	Experimental	20.1 (27.6)	37.6 (24.3)	1.09 (0.99, 1.20)	0.059
	Control	21.4 (36.0)	25.1 (19.9)	0.94 (0.87, 1.02)	0.134
Number of people with comorbidities		8.1 (51.4)	0.0 (0.0)	0.55 (0.41, 0.73)	<0.001
Multiple or single joint OA	Single	109 (76.8)	61 (83.6)	1.03 (0.60, 1.75)	0.925
	Multiple	32 (22.5)	9 (12.3)		
	Unsure	1 (0.7)	3 (4.1)		
Location of recruitment	Community	90 (63.4)	36 (49.3)	1.42 (1.07, 1.89)	0.016
	Hospital	32 (22.5)	20 (27.4)		
	Both	12 (8.5)	5 (6.9)		
	Not state	8 (5.6)	12 (16.4)		
Intervention (experimental) type	Pharmacological	66 (46.5)	46 (63.0)	0.50 (0.29, 0.88)	0.017
	Rehabilitation	74 (52.1)	27 (37.0)		
	Both	1 (0.7)	0 (0.0)		
	Unsure	1 (0.7)	0 (0.0)		
Intervention (control) type	Sham	63 (44.4)	36 (49.3)	0.80 (0.46, 1.40)	0.439
	Active Intervention	78 (54.9)	37 (50.7)		
	Both	1 (0.7)	0 (0.0)		
Number of sites	Single site	67 (47.2)	28 (36.4)	1.85 (1.17, 2.92)	0.009
	Multiple site	71 (50.0)	32 (43.8)		

	Unsure	4 (2.8)	13 (17.8)		
Sample size calculation met	Yes	83 (58.5)	35 (48.6)	1.44 (1.04, 2.00)	0.028
	No	29 (20.4)	9 (12.5)		
	Unsure	30 (21.1)	28 (38.9)		
Number of recruitment sites		10.2 (25.3)	9.7 (43.3)	0.99 (0.99, 1.01)	0.924
Duration of follow-up		8.5 (9.4)	5.5 (7.7)	0.95 (0.91, 0.99)	0.025

CI – confidence interval; N – number of participants; NRS – numerical rating scale; OA – osteoarthritis; OR – odd ratio; P – probability value; VAS – visual analogue scale

Table 3: Regression analysis on study characteristic factors related to follow-up rate

		Follow-up rate		Odd Ratio (95% CI)	P-Value
		<90% (N=93)	90%> (N=122)		
Location of OA	Hip	77 (82.8)	111 (91.0)	0.61 (0.36, 1.01)	0.054
	Knee	6 (6.5)	6 (4.9)		
	Hip and Knee	10 (10.8)	5 (4.1)		
Source of funding	Non-commercial	19 (20.4)	21 (17.2)	1.29 (0.99, 1.67)	0.059
	Commercial	52 (55.9)	57 (46.7)		
	None	5 (5.4)	8 (6.6)		
	Unclear	17 (18.3)	35 (28.7)		
	Commercial and non-commercial	0 (0.0)	1 (0.8)		
Education status	<High School	14.0 (49.7)	6.8 (19.6)	0.99 (0.99, 1.01)	0.720
	>College/University	15.9 (54.0)	4.6 (27.7)	0.99 (0.98, 1.00)	0.202
	No education	0.5 (3.6)	0.5 (3.3)	0.99 (0.92, 1.08)	0.966
Ethnicity	White/Caucasian	57.5 (171.7)	18.6 (72.0)	0.99 (0.99, 1.00	0.064
	Black/African American	7.3 (29.6)	3.0 (19.2)	0.99 (0.98, 1.01)	0.308
	Asian	1.5 (11.0)	2.7 (22.1)	1.01 (0.95, 1.05)	0.416
	Hispanic	0.2 (1.0)	0.2 (1.3)	1.18 (0.85, 1.62)	0.323
Age	Experimental	60.6 (4.2)	61.9 (6.3)	1.10 (0.96, 1.25	0.168
	Control	61.1 (4.3)	62.3 (5.2)	0.97 (0.85, 1.01)	0.629
Gender	Male	77.5 (94.7)	56.5 (67.8)	0.99 (0.99, 1.00)	0.731
	Female	131.7 (188.9)	87.0 (86.4)	0.99 (0.99, 1.00	0.168
Pain: VAS	Experimental	36.4 (66.3)	31.8 (26.9)	1.20 (1.02, 1.41)	0.031
	Control	28.3 (26.6)	30.2 (26.3)	0.84 (0.72, 0.99)	0.037
Pain: KOOS-HOOS	Experimental	49.8 (23.4)	53.8 (12.8)	1.38 (0.98, 1.95)	0.069
	Control	51.0 (21.2)	49.9 (15.8)	0.74 (0.53, 1.04)	0.081
Pain: WOMAC	Experimental	42.2 (81.6)	23.7 (25.6)	0.95 (0.86, 1.20)	0.680
	Control	42.6 (81.7)	24.1 (27.2)	1.04 (0.83, 1.30)	0.720
Pain: NRS	Experimental	17.0 (20.4)	29.7 (30.5)	1.05 (0.95, 1.17)	0.315
	Control	17.6 (21.4)	29.7 (37.7)	0.94 (0.89, 1.05)	0.502
Number of people with comorbidities		9.4 (62.1)	2.3 (12.9)	0.99 (0.99, 1.00)	0.285
Multiple or single joint OA	Single	77 (82.8)	93 (76.2)	1.28 (0.75, 2.20)	0.364
	Multiple	14 (15.1)	27 (22.2)		
	Unsure	1 (1.1)	2 (1.6)		
Location of recruitment	Community	58 (62.4)	68 (55.7)	1.21 (0.91, 1.61)	0.195
	Hospital	20 (21.5)	32 (26.2)		
	Both	11 (11.8)	6 (4.9)		
	Not state	4 (4.3)	16 (13.1)		
Intervention (experimental) type	Pharmacological	50 (53.8)	62 (80.8)	1.06 (0.64, 1.75)	0.827
	Rehabilitation	42 (45.2)	59 (48.4)		
	Both	0 (0.0)	1 (0.8)		
	Unsure	1 (1.1)	0 (0.0)		
Intervention (control) type	Sham	50 (53.8)	49 (40.2)	1.63 (0.95, 2.79)	0.074
	Active Intervention	42 (45.2)	73 (59.8)		
	Both	1 (1.1)	0 (0.0)		
Number of sites	Single site	40 (43.0)	55 (45.1)	1.17 (0.76, 1.81)	0.472
	Multiple site	50 (53.8)	53 (43.4)		

	Unsure	3 (3.2)	14 (11.5)		
Sample size calculation met	Yes	43 (46.2)	75 (62.0)	0.86 (0.63, 1.17)	0.332
	No	27 (29.0)	11 (9.1)		
	Unsure	23 (24.7)	35 (28.9)		
Number of recruitment sites		16.8 (43.8)	4.4 (12.3)	0.98 (0.96, 0.99)	0.026
Duration of follow-up		9.4 (8.9)	6.1 (8.8)	0.96 (0.92, 0.99)	0.015

CI – confidence interval; N – number of participants; NRS – numerical rating scale; OA – osteoarthritis; OR – odd ratio; P – probability value; VAS – visual analogue scale

Supplementary Table 1: Pubmed search strategy

1. Exp. Hip
2. Exp. Knee
3. Exp. Osteoarthritis
4. (((randomised[Title/Abstract]) OR (random[Title/Abstract])) OR (comparator[Title/Abstract])) OR (clinical trial[Title/Abstract])
5. Date restrict:2013-2021.