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

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Abstract

Background: The prevalence of osteoarthritis (OA) increases with age, growing by approximately three percent annually. There are multiple treatment options available to reduce symptoms, including pharmacological, non-pharmacological, surgical and alternative interventions. Research is paramount to ensure this growing population has access to evidence-based interventions. High attrition (greater than 20%) and failure to recruit a predetermined sample size for statistical power result in inefficient trial designs, delaying or preventing answers to the original clinical questions with adequate power and precision.

Aims: To identify recruitment and retention rate in randomised controlled trials (RCTs) recruiting individuals with hip or knee osteoarthritis (OA) and to determine the factors that influence these rates.

Material and methods: PubMed search identified RCTs published between 2013 and 2021 that involved people with hip or knee OA. Regression analyses determined factors related to participants and the trial that may have affected recruitment or retention rates.

Results: 215 RCTs were included in the study. 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 recruit individuals 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), were 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 that impact patient 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.

Key words

RCT, design efficiency, recruit, follow-up, attrition, osteoarthritis.

Introduction

Randomised controlled trials (RCTs) remain the methodological gold standard in intervention research. Patient recruitment remains a key element in 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. Survey conducted by Duley et al. [2], among the UK Clinical Research Collaboration (UKCRC) registered Clinical Trials Units, reported that recruitment inefficiency was the main reason for not meeting recruitment targets. Similarly, Huang et al. [1] reported that 86% of RCTs failed to recruit their target number of participants within the planned timeframe, with 19% and 19% of RCTs terminated prematurely due to insufficient recruitment [1]. This challenges of recruitment and retention of trial participants jeopardizes the completion of important clinical research while also being inefficient in relation to time and resources for funders, research participants, clinicians, and patients [3,4]. Thus, this is considered a research 'waste' [5,6].

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

Enrollment rates in osteoarthritis clinical trials are relatively low [5,6]. Trials frequently fail to meet recruitment targets [5,6]. Approximately 85% of clinical trials fail to reach their recruitment targets within the planned timeframe [1], with 19% terminating before reaching the target sample size [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 failure to recruit a predetermined sample size for statistical power result in inefficient trial designs, delaying or preventing answers to the original clinical questions with adequate power and precision.

Aims

It is uncertain what factors affect patient recruitment and retention rates and their efficiency in osteoarthritis trials. The aim of this study was to identify the recruitment and retention rates in osteoarthritis RCTs published between 2013 and 2021, and to investigate possible factors influencing these rates. This is important as the findings of this analysis will provide insights into strategies that may improve recruitment, and therefore contribute to the effectiveness of future recruitment and retention strategies in clinical trials involving individuals with osteoarthritis.

Materials and methods

We undertook a bibliometric analysis to assess factors influencing recruitment and retention of participants in osteoarthritis research. Studies published between January 2013 and January 2021 were identified through the PubMed search engine. The search strategy was presented in **Supp. Table 1.** Studies were included if they were: RCTs recruiting people with hip and/or knee osteoarthritis; presented as full-text publications. Studies were excluded if they were: publications that provided 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 search result titles and abstracts. The two reviewers independently screened all potentially eligible studies at full-text level. Only studies that met the

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.

eligibility criteria agreed upon by two reviewers were included in the study. Disagreement regarding 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). Extracted data included: number of participants; location of osteoarthritis; sample size; country of origin; source of funding; number of screened participants; number of participants assessed at last assessment; participants' 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. If disagreements occurred during data extraction, they were resolved through discussion, adjudicated by a third reviewer (TS).

Data analysis

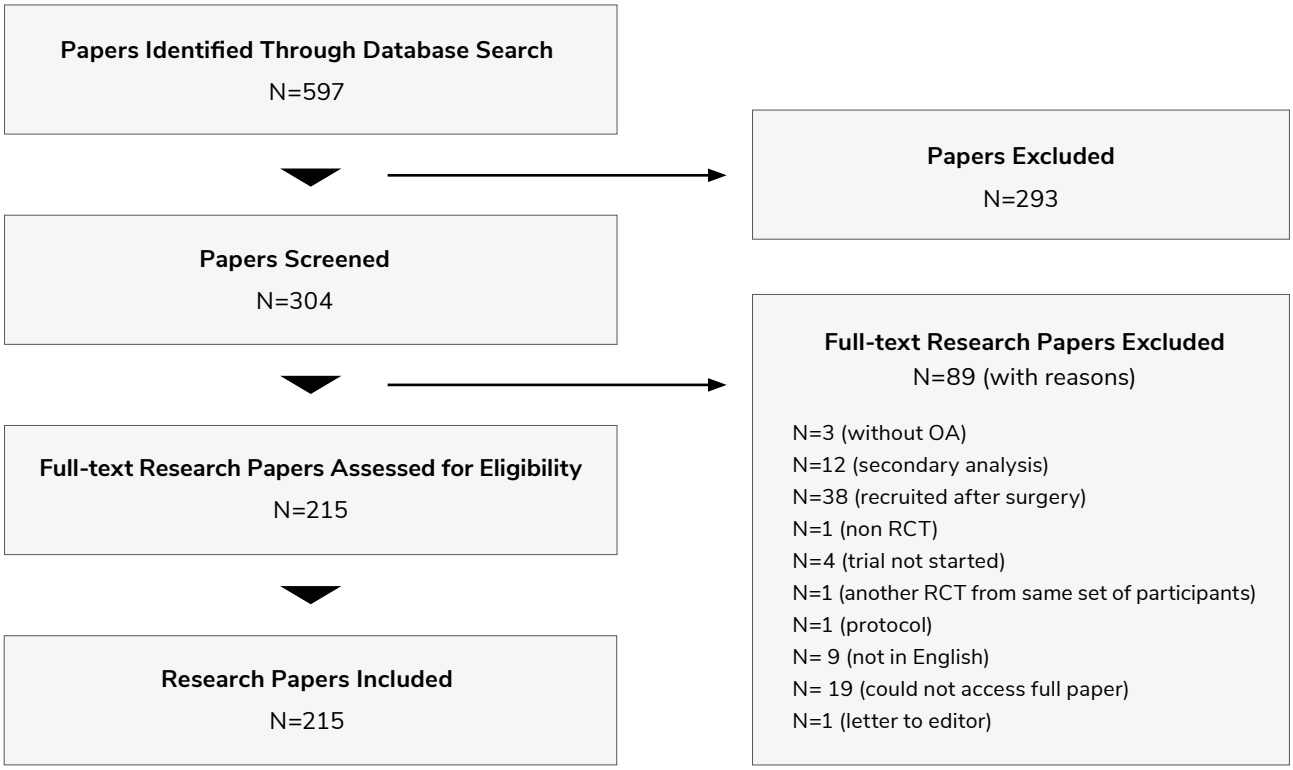
An assessment of data normality was performed using the Kolmogorov-Smirnov test. Data were descriptively analysed using mean and standard deviation (SD) values for continuous data, frequency and percentages for categorical data. The randomisation rate was expressed as the number of participants randomised 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 of randomized participants. Subgroup analyses were conducted using regression analyses in which arbitrary cut-off 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 considered to show a significant association when the p-value was <0.05. All statistical analyses were carried out using STATA version 16.0 (Stata Corp, Texas, USA).

Results

Participant and study characteristics

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

Figure 1. Study flow chart.



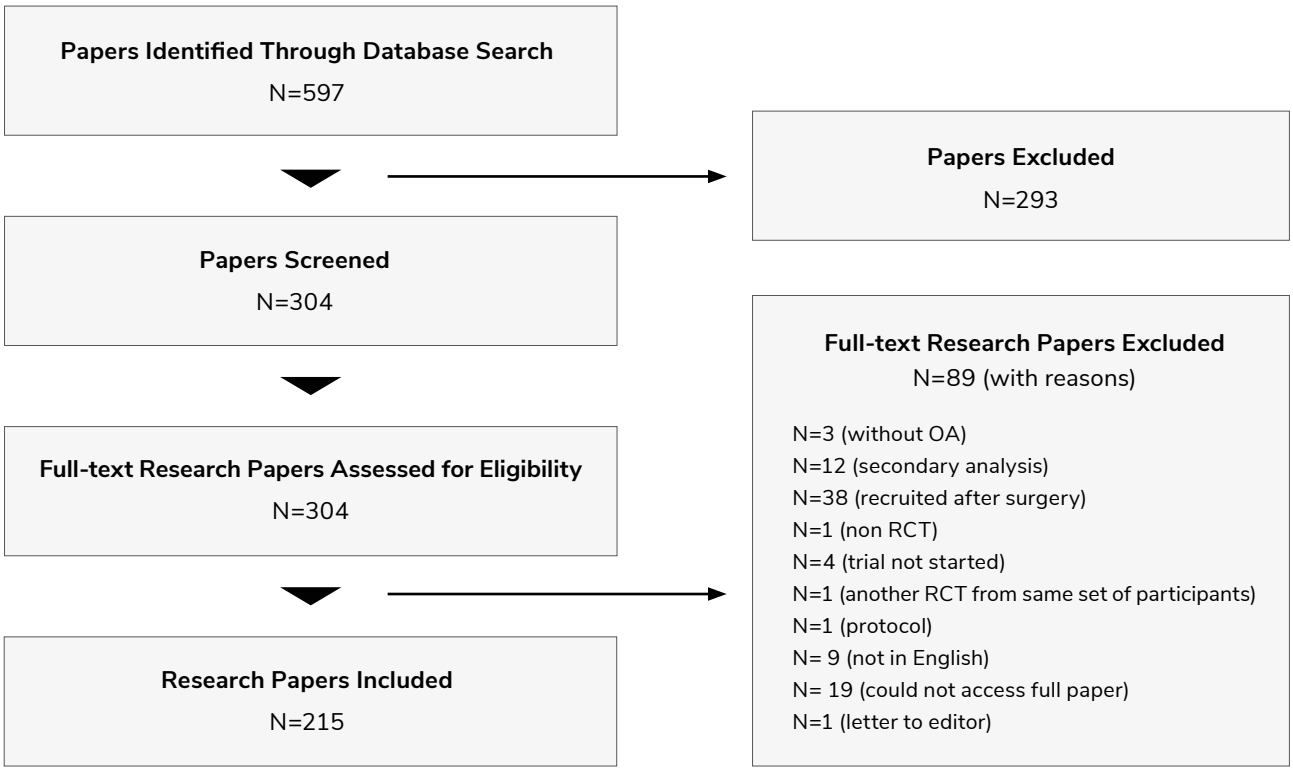


Table 1. Demographic characteristics.

		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)

Country of origin	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)

Ethnicity	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

Abbreviations: 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.*

Recruitment rate

Seven factors were identified as being significantly associated with recruitment rates (**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 recruited people with medical comorbidities (OR: 0.55; 95% CI: 0.41, 0.73; p<0.001) were less likely to have a recruitment rates 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 that recruited from hospitals were more likely to have a recruitment rate above 80% when compared to those that recruited from community sources (OR: 1.42; 95% CI: 1.07, 1.80; p=0.016). Trials that offered pharmacological interventions 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 the number of sites (p=0.009) and whether studies met their sample size criteria (p=0.028), the differences in the actual numbers of studies that recruited 80% or more of their screened participants was minimal **(Table 2)**.

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)		

Source of funding	Unclear	24 (16.9)	28 (36.4)	1.47 (1.12, 1.92)	0.005
	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)		

Intervention (experimental) type	Unsure	1 (0.7)	0 (0.0)	0.50 (0.29, 0.88)	0.017
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

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

Follow-up rate

Four factors were identified as being significantly associated with a follow-up rate of 90% or more **(Table 3)**. All other examined factors were found to be statistically insignificant. Research in which the experimental group had 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 shown when controlled participants had higher pain scores (OR: 0.84; 95% CI: 0.72, 0.99; p=0.037). Studies that 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 when compared to trials with a higher number of sites and longer follow-up duration **(Table 3)**.

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)		

Source of funding	Unclear	17 (18.3)	35 (28.7)	1.29 (0.99, 1.67)	0.059
	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)		

Intervention (experimental) type	Unsure	1 (1.1)	0 (0.0)	1.06 (0.64, 1.75)	0.827
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

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

Discussion

The findings of this analysis indicate that conversion of screening to randomisation in trials involving individuals with hip and/or knee osteoarthritis was moderately high (mean: 63%) and equally high for follow-up rates (88%) after an average of eight months. Studies 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 had lower pain scores at baseline, but control participants had higher scores, recruited from fewer sites, and had a shorter follow-up duration. These findings may be helpful in planning clinical trials involving people with osteoarthritis, allowing for the design of more effective studies.

Individuals with osteoarthritis frequently present with various medical comorbidities [17]. They are approximately three times more likely to have multiple comorbidities when 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 rates were lower in trials that recruited people with medical comorbidities. Given the high proportion of individuals with medical morbidities in this population, excluding them from trials for this reason poses external validity issues [18]. However, these results may be partially explained by the hypothesis that people with other morbidities may withdraw from the study due to other time commitments associated with managing comorbidities [19], different views of health priorities over osteoarthritis when compared to other comorbidities [20], or selection bias against individuals with medical comorbidities. Although beneficial for recruitment rates, the generalizability trade-off achieved by excluding those with comorbidities does not justify this exclusion criterion.

There was a difference in recruitment and follow-up rates dependent on the type of examined interventions. Trials investigating pharmacological interventions as their experimental treatment were more likely to recruit over 80% of those screened. This may be partially related to individual's willingness to participate in a pharmacological trial where participation in the intervention may be less time-consuming than in a rehabilitation trial. This contrasts with the notion that individuals may associate drug trials with the risk of adverse events [21,22]. Nonetheless, the findings suggest that special attention should be given to improving recruitment rates for non-drug trials in people with osteoarthritis, particularly given that rehabilitation is considered the primary intervention in this population [23].

Trials with follow-up rates of 90% or above reported that their experimental group had lower pain scores and their control group had higher pain scores. Accordingly, higher attrition was reported when participants in the experimental group had higher preoperative pain scores and the control group had lower scores. Attitudes towards treatment allocation and the perceived intervention effect, particularly for unblinded trials, may have determined whether an individual continued to follow-up. Previous literature has suggested that people with osteoarthritis have lower compliance to prescribed treatments when compared to the population with other long-term conditions, such as heart-disease [20,24]. This viewpoint of the disease may be one of the reasons for attrition, depending on symptoms level. Therefore, measures to support continued participation in osteoarthritis research are particularly pertinent for participants depending on their baseline symptoms.

Publicly funded trials were more likely to have a recruitment rate of 80% or above when compared to commercially funded research. Most data to date on participant recruitment and retention factors have 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 osteoarthritis research, has explored both commercially and publicly funded trials, indicating a difference. This may be attributed to participant's attitudes toward commercially funded research, potentially demonstrating reduced willingness to participate due to less altruistic motivations or suspicion of financial gain to the commercial partner [27]. Alternatively, this may reflect differences in the site's 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 approaches can be used in the way commercial trials are communicated and delivered to participants to mitigate this difference in recruitment rates.

Whilst this trial identified several factors associated with recruitment and retention, it did not set out to explore strategies that could improve them. Several Cochrane reviews have identified methods such as telephone reminders, open (unblinded) study designs, financial incentives, and online data collection as potential factors which could be used [29-31]. These potential approaches can be considered to address some of the risks identified in this study with respect to recruitment and retention.

Strengths and limitations

A strength of this study is that it is the only analysis that investigated whether certain variables influence recruitment and retention of participants in musculoskeletal research. However, there are several important limitations. Firstly, we only included English-language publications. Consequently, nine papers were excluded. Secondly, we only searched the PubMed database. This was justified, as it was anticipated to provide an appropriate source of published RCTs. However, it is acknowledged that this is therefore not a systematic review which could have provided a more comprehensive analysis of the evidence base. Thirdly, data were not consistently reported in each paper. Some papers reported a small num-

ber of variables, while others presented a greater range of variables. Therefore, data were limited for some variables. For instance, 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 that recruited individuals after surgical procedures were not included. This was justified on the grounds that those who underwent the surgery had resolved their osteoarthritis symptoms. However, surgery is one of the key treatments for osteoarthritis, and is therefore worth further investigation.

Conclusions

Recruitment and follow-up rates in studies involving 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 higher follow-up rates if their experimental group had lower pain scores at baseline, but controlled participants had higher scores, are recruited from fewer sites, and have shorter follow-up duration. These findings may help develop more effective strategies for patient recruitment and retention in future osteoarthritis trials. This will help increase the efficiency of conducting research, thereby reducing research waste, so that reliable answers to these important research questions for people with joint pain can be obtained more swiftly.

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