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The feasibility of an exercise intervention to improve sleep (time, quality and disturbance) in people with rheumatoid arthritis: a pilot RCT

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Abstract

Current rheumatology guidelines recommend exercise as a key component in the management of people with RA, however, what is lacking is evidence on its impact on sleep. Objective is to assess the feasibility of a walking-based intervention on TST, sleep quality, and sleep disturbance and to generate potential effect size estimates for a main trial. Participants were recruited at weekly rheumatology clinics and through social media. Patients with RA were randomized to a walking-based intervention consisting of 28 sessions, spread over 8 weeks (2–5 times/week), with 1 per week being supervised by a physiotherapist, or to a control group who received verbal and written advice on the benefits of exercise. Primary outcomes were recruitment, retention, protocol adherence and participant experience. The study protocol was published and registered in ClinicalTrials.gov NCT03140995. One hundred and one (101) people were identified through clinics, 36 through social media. Of these, 24 met the eligibility criteria, with 20 randomized (18% recruitment; 100% female; mean age 57 (SD 7.3 years). Ten intervention participants (100%) and eight control participants (80%) completed final assessments, with both groups equivalent for all variables at baseline. Participants in the intervention group completed 87.5% of supervised sessions and 93% of unsupervised sessions. No serious adverse events were related to the intervention. Pittsburgh Sleep Quality Index global score showed a significant mean improvement between the exercise group-6.6 (SD 3.3) compared to the control group-0.25 (SD 1.1) ($p=0.012$); Intervention was feasible, safe and highly acceptable to study participants, with those participants in the exercise group reporting improvements in sleep duration and sleep quality compared to the control group. Based on these findings, a fully powered randomized trial is recommended. Trial registration number: ClinicalTrials.gov Identifier: NCT03140995 (April 25th, 2017)

Keywords Inflammatory arthritis · Physical activity · Sleep quality · Sleep duration · Accelerometer

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Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune condition that can lead to reduced activity levels in up to 60% of participants [1]. Poor sleep quality is prevalent in people with RA [2] with 40–64% of participants reporting reduced Total Sleep Time (TST) [3, 4].

Results from a recent systematic review could find no strong evidence for the effect of exercise on sleep in people with RA, partly due to the small number of studies ($N=5$) available [5]. In addition, the lack of studies of the highest methodological quality complicates the interpretations of the findings, therefore, the most effective exercise prescription in terms of the Frequency, Intensity, Time and Type (FITT) principle, and the ideal approach to exercise delivery, requires further research.

Evidence indicates that sleep is an essential aspect in maintaining the body's circadian rhythm and maintaining health-related quality of life (HRQoL), therefore, sleep disturbances could have a detrimental impact on same in people with RA. Various sleep organisations support TST figures, with the American Academy of Sleep Medicine (AASM) and the Sleep Research Society (SRS) recommending adults sleep at least 7 h per night to promote optimal health and well-being [6], while the National Sleep Foundation (NSF) adults/older adults advocate a 'sleep needs spectrum' of 7–9 h sleep per night. This 'spectrum' is necessary, as sleep has a role to play in our immune system and is also important in the restoration and maintenance of homeostasis. Sleep disorders and reduced TST may lead to the development of autoimmune diseases like RA, due to the triggering of autoantibody production [7].

With sleep being identified as a major concern for people with RA, and disturbed sleep and fatigue known to affect up to 70% in this population [8], health professionals (HPs) should be concerned with the effect low TST and poor sleep quality has on HRQoL. Low TST and poor sleep quality, in addition to their effect on mental and physical health [9, 10], may lead to people with RA being less active [11]. Therefore, aiming to increase TST and improving sleep quality through exercise, may be a health promotion strategy that is feasible and safe for this population. As exercise prescription is a core skill for some HPs e.g. physiotherapists, they should play an important role in educating patients on the benefits of increasing their exercise levels [12], and its potential positive effect on sleep, however, based on research to date, interventions are required to show an effect [5].

A number of studies have investigated the effects of aerobic exercise on TST and sleep quality in other populations and while results suggest they are beneficial, it is unclear how large these benefits are [13, 14]. Cross-sectional self-report and objective studies in people with RA indicate a population with low TST, along with those who are more active indicating a longer TST, supports the need to further this area of research to test for effect [4, 12]. Exercise is recommended as a key component in the management of people with RA [15, 16], however, what is lacking is evidence of its impact on TST and sleep quality [5, 17].

It has been well established that being physically active and taking regular exercise are important for those who have been diagnosed with RA across the lifespan [18]. Research has shown that people with RA may benefit from several forms of exercise [19], which are safe and beneficial conferring benefits at low risk to people with RA [20]. However, adherence to exercise is often low or unrecorded [12], raising questions about the feasibility and acceptability of some forms of aerobic exercise in people with RA and, in particular, for improving TST and sleep quality.

Walking is an ideal form of aerobic exercise owing to its ease of accessibility and relatively low impact, with a low risk of musculoskeletal injury [21]. Low-to-moderate intensity walking has been shown to lead to improvements in aerobic capacity and body mass index [22]. Walking is, therefore, a low-cost and simple form of exercise, requiring little formal training and has been found to be feasible, acceptable and safe, for people with RA [23]. Previous studies have used walking as an exercise intervention for people with arthritis and have involved a non-randomized control (non-RCT) trial design, or have focused on community samples with self-reported diagnoses of arthritis [24]. A 2016 pilot RCT demonstrated that people with RA found their walking intervention feasible and acceptable as they participated in the required number of sessions per week [23]. Furthermore, the authors reported their intervention safe, as no adverse events (AEs) were reported and pain levels did not differ between the intervention and control groups. These findings concur with previous systematic reviews [25] which showed that AEs are rare for people with RA who participate in PA and exercise. Together, these findings should provide encouragement and reassurance to HPs, recommending walking as an aerobic exercise for people with RA. However, the potential role of walking as an exercise intervention in the management of RA, specifically to improve TST and sleep quality, has yet to be studied.

High-quality research is required to inform and implement evidence-based practice (EBP) [26], which requires an appropriate study design to answer the research question [27]. To investigate the effect of various types of interventions, like PA and exercise, randomized controlled trials (RCT) are recognized as the gold standard for study designs [28]. The successful development and implementation of an RCT can encounter many barriers from a design perspective and, therefore, it is prudent to undertake pilot work prior to fully engaging in a large study. The second phase of the

Medical Research Council (MRC) framework recommends pilot studies to investigate the feasibility of the study design in the intended population and highlight any barriers to the success of a larger scale trial [29], thereby reducing research waste in exercise interventions. Therefore, the aim of this study is to assess the feasibility of a walking-based intervention to improve sleep (time, quality, and disturbance), in people with RA to inform an RCT.

Materials and methods

Study design

The design was a single blinded pilot RCT of a walking-based exercise intervention against information on the benefits of exercise for an 8-week period. All outcome measures were collected by a researcher blinded to the intervention (LC). The exercise intervention was delivered by the first author (SMcK) who is a chartered physiotherapist. Participant characteristics and outcome assessments were collected by the blinded assessor at baseline (T1) and 1-week post-intervention (T2). The study protocol was published [30] and registered in ClinicalTrials.gov NCT03140995.

Screening using the Pittsburgh Sleep Quality Index (PSQI) [31] was used to clarify whether participants fulfilled the criteria for poor sleep (PSQI global score > 5), and to ascertain their physical activity levels. Participants completed a consent form and were free to withdraw at any time. While no compensation was provided, participants were equipped with a 'High Visibility Vest', which is a piece of clothing that is highly luminescent in its natural matt property or a colour that is easily discernible from any background. This was provided for safety due to the intervention taking place in the late Autumn/early Winter.

Participant recruitment

A sample of convenience was used with participants meeting the inclusion and exclusion criteria (Table 1) being identified through weekly rheumatology clinics or contacted through social media.

Ethics

Approval was obtained from the Research Ethics Committee at a University Hospital (REC: 60/17) and procedures performed in the study involving human participants were in accordance with the ethical standards of the University and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Participants completed a consent form and were free to withdraw at any time. The reporting of results are recorded in accordance with the Consolidated Standard of Reporting trials (CONSORT) for pilot trials [32].

Intervention and control group

The exercise intervention is outlined in Table 2 and was a walking-based exercise intervention based on the American College of Sports Medicine (ACSM) aerobic exercise guidelines [33], which is similar to that as recommended by the

Table 1 Inclusion and exclusion criteria

Inclusion criteria
Participants to have a confirmed diagnosis of RA based on the ACR/EULAR criteria
Aged over 18 years or over
Provide informed consent, understand and speak English
Do not participate in regular physical activity in their leisure time (self-reported aerobic exercise < 5 times per week)
Poor sleep (PSQI > 5)
Low disease score on 28 joints (DAS28-CRP)
Health assessment questionnaire (HAQ) < 2.4
NYHA functional classification I or II
Exclusion criteria
Severe physical disability (HAQ) > 2.5
Pregnancy
High disease score on 28 joints (DAS28-CRP)
Participate in regular physical activity in their leisure time (self-reported aerobic exercise > 5 times per week)
NYHA functional classification III or IV

ACR American College of Rheumatology, *EULAR* European League Against Rheumatism, *PSQI* Pittsburgh Sleep Quality Index, *DAS-28* Disease Activity Score 28, *HAQ* Health Assessment Questionnaire, *NYHA* New York Heart Association

Table 2 Exercise intervention

Pilot RCT Exercise training program for people with RA—walking intervention (8 weeks)					
	Supervised/unsupervised sessions	Detail		Supervised/unsupervised sessions	Detail
Week 1	1 Supervised session; 1 Unsupervised session	5 min warm-up; 20 min walking (RPE 11); 5 min cool-down; dynamic stretching	Week 5	1 Supervised session; 3 Unsupervised sessions	5 min warm-up; 30 min walking (REP 13); 5 min cool-down; dynamic stretching
Week 2	1 Supervised session; 1 Unsupervised session	5 min warm-up; 20 min walking (RPE 11); 5 min cool-down; dynamic stretching	Week 6	1 Supervised session; 3 Unsupervised sessions	5 min warm-up; 30 min walking (RPE 14); 5 min cool-down; dynamic stretching
Week 3	1 Supervised session; 2 Unsupervised sessions	5 min warm-up; 25 min walking (RPE 12); 5 min cool-down; dynamic stretching	Week 7	1 Supervised session; 4 Unsupervised sessions	5 min warm-up; 40 min walking (REP 15); 5 min cool-down; dynamic stretching
Week 4	1 Supervised session; 2 Unsupervised sessions	5 min warm-up; 25 min walking (REP 12); 5 min cool-down; dynamic stretching	Week 8	1 Supervised session; 4 Unsupervised sessions	5 min warm-up; 40 min walking (RPE 15); 5 min cool-down; dynamic stretching

RPE Rate of Perceived Exertion (Borg 6–20)

World Health Organisation [34] and recent European League against Rheumatism (EULAR) PA guidelines [18], of being moderate intensity (50–80% of HRR) for at least 30 min on 5 or more days, for a total of 150 min per week. The supervised sessions were group based, while the unsupervised sessions were performed by the participant at a time and location of their choice.

As participants would not be meeting the relevant PA guidelines, the programme was devised using incremental targets for daily walks and participants were advised to monitor and progress their exercise intensity using the Borg Rating of Perceived Exertion (BORG) (RPE) scale (range 6–20) [35]. Participants were instructed to be moderately short of breath on exertion and were encouraged to maintain an RPE of 12–17 (equivalent to 50–80% of maximal exertion). This scale is a frequently used quantitative measure of perceived exertion during exercise [36] and has been found to be highly correlated with heart rate, lactate levels, %VO2max, and breathing [37]. Studies have supported the validity of the RPE scale in a wide range of populations, including inflammatory arthritis [38]. In addition, participants' cardiorespiratory fitness was assessed using a submaximal treadmill test, i.e. modified Bruce protocol, which is walking based and involves walking at an increasing gradient, stopping at a HR/RPE threshold [39].

Participants were advised to seek medical assistance if there was adverse reaction during the intervention e.g. flare-up, fall, or if the participant feels unwell.

Randomization and blinding

Randomization was performed by computer generated random numbers with a 1:1 allocation ratio. Allocations were stored in a locked cabinet and an envelope was handed to participants after completion of their baseline assessments. Each envelope contained a code number, which participants used on all outcome assessments in place of their names.

Primary outcomes

Recruitment

As this is a pilot study, sample size calculations were not required [40]. The target recruitment was 40 participants, which was considered to be a realistic target for the timeframe available (3 months) and was a similar sample size to other pilot RCTs in people with RA [2, 23, 41]

Retention

Conservative rate of 80%, which is established a priori as acceptable for this type of study [17]

Protocol adherence

Attendance at weekly supervised sessions; completion of a weekly exercise log for the unsupervised part and completion of a weekly National Sleep Foundation's (NSF) sleep diary. Accepted levels of adherence were based on the nature and frequency of reported attendance, with data being reported for those who completed and did not complete the intervention with a priori level of 80%.

Participant experience

According to the protocol [30], a qualitative evaluation was conducted using semi-structured face-to-face interviews. These will be reported separately.

Safety

Primary safety outcomes included the type and frequency of adverse events (AEs) [42].

Secondary outcomes

Physical activity profile

This was quantified using an activPAL3 accelerometer continuously worn on the right thigh by the participants for 8 days, beginning week 1 before start of intervention and for 8 days 1 week post-intervention [43], with the first 24 h were not included in the analysis to minimise the effects reactivity. Though an 8-day wear-time was employed, the first 24 h were not included in the analysis to minimise the effects reactivity to wearing the device. A minimum recording duration of 3 days from the last 7, including at least 1 weekend day was required for data processing; samples of lower than 3 days were not included. Recordings were processed for daily minutes of moderate to vigorous physical activity (MVPA). The activPAL activity monitor, classifies an individual's free-living activity into periods spent in sedentary, standing, and walking behaviours through the use of proprietary algorithms. It has been found to be a reliable and valid measure of sedentary and physical activity behaviours and transition and step counts in other populations [44, 45], including adults who are healthy and adults who are overweight, in addition to walking behaviours in people with RA [46].

Sleep

Measured using the Pittsburgh Sleep Quality Index (PSQI) [31], with sleeping pattern measured by the National Sleep Foundation's (NSF) Sleep Diary. The PSQI measures TST, sleep quality, sleep latency, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction over the last month.

Pain (RA)

Measured with a 10 cm visual analogue scale (VAS), which has good reliability and validity, and is sensitive to detecting changes in pain in inflammatory conditions [47].

Mood

Which includes depression and anxiety, measured by the Profile of Mood States questionnaire (POMS) [48], which has an internal consistency of 0.63–0.96 Cronbach alpha rating; Quick Inventory of Depressive Symptomatology (QIDS-SR16) [49], which has an internal consistency of 0.86 Cronbach alpha and has high concurrent validity and the State Trait Anxiety Inventory (STAI) [50], which has an internal consistency ranging from 0.86 to 0.95.

Functional limitation

Measured by the Health Assessment questionnaire disability index (HAQ-DI), which is the most commonly used measure of functional disability in RA and has good-to-excellent reliability and validity [51].

Disease activity: evaluated using the Clinical Disease Activity Index (CDAI) which has been implemented and validated for RA using several clinical trial datasets [52].

Health-related Quality of life: measured by EuroQoL, which measures health-related quality of life and contains five dimension, with each dimensions having five levels from 'no problems' to 'extreme problems' [53].

Fatigue

Measured by the Bristol Rheumatoid Arthritis Fatigue Multi-Dimensional Questionnaire (BRAF-NS) [54]. This measures the impact of fatigue for people with RA and disease specific and has acceptable to good convergent validity.

Barriers to exercise

Evaluated using the Exercise Benefits and Barriers Scale (EBBS) [55].Validation studies show internal consistencies between 0.80 and 0.94.

Data analysis

Scoring of the standardized questionnaires was carried out according to the guidelines from the instrument developers with participant code numbers ensuring blinding of data analysis. Data were double entered Microsoft Office

Excel (2013), which was used for descriptive analysis of demographic questions. Categorical data were described using counts and percentages. As recommended, continuous data presented using medians and interquartile ranges (IQR) whether they are normal or not [56]. A 5% level of significance was used for all statistical tests. Data analysis was undertaken in SPSS version 22 (IBM corporation, New York, USA) with activPAL version 7.2.32 being used for physical activity profile.

Results

Patient characteristics

Twenty-four (24) participants were recruited, with 4 withdrawing pre-assessment resulting in 20 randomised to the intervention ($N=10$) or control ($N=10$) (Fig. 1). Baseline demographic and clinical characteristics are reported in Table 3.

All participants were female, with a mean age of 57 (SD 7.5); mean RA diagnosis of 10.7 (SD 6.4) years; moderate-to-severe disability (HAQ-DI: 1.4 (SD 0.63). Participants were predominately married (85%), in employment (55%), and educated to third level (50%). Biological Disease-modifying antirheumatic drugs (DMARDS) were taken by 75%, with 50% taking sleep medications, either 'prescribed or over the counter'.

The DAS28 score was noted but not recorded for this study, however, it should be for any future trial.

Primary outcome measures

Recruitment

137 participants were invited to join the study, of whom 58 (42%) expressed interest and were screened for eligibility. Thirty-four (34) were excluded at assessment with the remaining 24 meeting all eligibility criteria and were recruited, with 20 being randomised. The final recruitment rate was 18% and all were female.

Retention

Participant retention exceeded the a priori level of 80% at baseline (100% intervention and control) and primary time point (100% for intervention; 80% for control).

Protocol adherence

Supervised sessions For the supervised sessions, participant attendance was 87.5%, with a mean of 9 (SD 2) sessions across the group.

Unsupervised sessions For the unsupervised part, the participants' exercise log indicated 93% completed, with a mean of 18.5 (SD 4) sessions.

Sleep diary Poor compliance with the NSF's sleep diary, with many missing values in the data, made it difficult to analyse.

Adverse events

Participants reported several adverse events (AEs) during the 8-week intervention period; however, none were serious. The most common AE was increased musculoskeletal pain, which was generally mild, short-term and located in the lower body (Table 4).

Power and sample size calculations

Based on the results from the PSQI with different SDs in each treatment group, a sample size of 18 in each group will have a 90% power to detect a difference in means of 3.000, assuming that the Group 1 SD is 3.500 and the Group 2 SD is 1.200 (ratio of Group 2 to Group 1 standard deviation is 0.343), using a two group Satterthwaite *t* test with a 0.050 two-sided significance level [57].

A sample size of 18 in each group will have a 90% power to detect a difference in means of 3.000, assuming that the common standard deviation is 2.620 using a two-group t test with a 0.050 two-sided significance level. This is the same result if we assume equal SDs in the groups [57].

These are both estimating the number needed to detect a difference of at least 3 (PSQI) between the groups. Assuming a drop-out rate of 30% provides a figure of 26 per group, however, if researchers think the dropout will be higher than this, then they should recruit more e.g. 30 per group.

Secondary outcome measures

Descriptive statistics for secondary outcomes are reported in Table 5.

Physical activity profile

Those in the Intervention group were meeting the ACSM activity guidelines pre-intervention (moderate intensity, for at least 30 min on 5 or more days, for a total of 150 min per week) of 152 min [IQR 93, 211]; there was no difference compared to the control group at baseline ($p=0.22$). Post-intervention, participants in the exercise group showed a significant improvement in their weekly MVPA ($p<0.003$). With regards to their fitness, both groups were comparable at baseline ($p=0.27$), with exercise participants significantly improving post intervention ($p<0.001$).

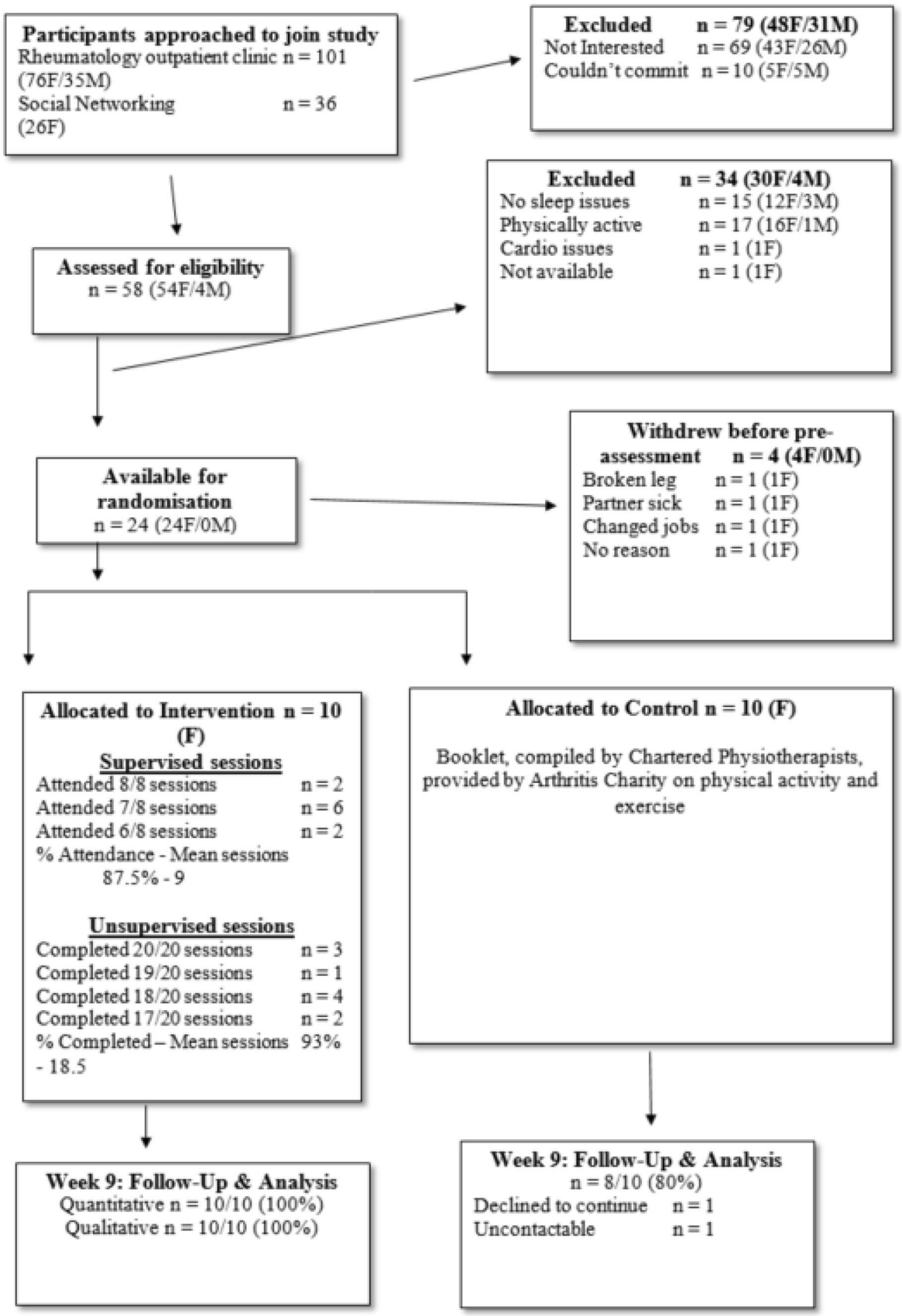

Fig. 1 Flowchart of participants through trial

Table 3 Participant demographics and clinical characteristics

Demographic	Group, *N* (%)			
	All ($n=20$)	Intervention ($n=10$)	Control ($n=10$)	*p*-value
Age (years), mean ± SD	57 ± 7.5	58 ± 7.4	56 ± 7.9	0.55
RA symptoms (years), mean ± SD	15.8 ± 7.2	14.1 ± 7.4	17.4 ± 6.7	
RA diagnosed (years), mean ± SD	10.7 ± 6.4	9.9 ± 7.0	11.5 ± 5.6	
Gender (male/female)	0/20 (100)	0/10 (100)	0/10 (100)	
Relationship status	*N* (%)			
Single	3 (15)	2 (20)	1 (10)	
Married	17 (85)	8 (80)	9 (90)	
Working situation	*N* (%)			
Full-time employment	3 (15)	1 (10)	2 (20)	
Part-time employment	8 (40)	5 (50)	3 (30)	
Disability pension	2 (10)	1 (10)	1 (10)	
Housewife/househusband	5 (25)	2 (20)	3 (30)	
Unemployed	1 (5)	0 (0)	1 (10)	
Retired (due to age)	1 (5)	1 (10)	0 (0)	
Education	*N* (%)			
Primary level	1 (5)	1 (10)	0 (0)	
Secondary level	9 (45)	3 (30)	4 (40)	
Third level	10 (50)	6 (60)	6 (60)	
Smoking status	*N* (%)			
Now smoking	3 (15)	2 (20)	1 (10)	
Used to smoke	11 (55)	5 (50)	6 (60)	
Take alcohol	16 (80)	8 (80)	9 (90)	
Type of RA medication	*N* (%)			
Biological DMARDS	15 (75)	7 (70)	8 (80)	
Non-biological DMARDS	3 (15)	2 (20)	1 (10)	
Do not take medication	1 (5)	0 (0)	1 (10)	
Do not know	1 (5)	1 (10)	0 (0)	
Sleep medication	*N* (%)			
None	10 (50)	5 (50)	5 (50)	
Prescribed	7 (35)	3 (30)	4 (40)	
Over the counter	3 (15)	2 (20)	1 (10)	
MVPA (minutes) median/IQR	139 (96, 198)	152 (93, 211)[a]	115 (83, 148)	0.22
PSQI eligibility score (0/21), mean ± SD	13.1 ± 2.7	13.4 ± 2.5	12.8 ± 2.8	0.64
$V0_2$max (ml/kg/min) mean ± SD	28.9 (4.8)	27.4 (5.4)[a]	30.1 (4.5)	0.27
BMI, mean ± SD	27 ± 5.6	27 ± 4.1	27 ± 7.1	0.96
HAQ	1.4 ± 0.63	1.5 ± 0.60	1.3 ± 0.66	0.60
CDAI	16.2 ± 5.0	16.7 ± 5.4	15.7 ± 4.6	0.65
NYHA classification	Class I = 17 Class II = 3	Class I = 9 Class II = 1	Class I = 8 Class II = 2	

RA Rheumatoid arthritis, *BMI* Body Mass Index, *CDAI* Clinical Disease Activity Index, *DMARDS* Disease-modifying antirheumatic drug, *PSQI* Pittsburgh Sleep Quality Index, *NYHA* New York Heart Association, *HAQ* Health Assessment Questionnaire, *MVPA* Moderate to vigorous physical activity, *NYHA* New York Heart Association classification

[a]Data available for 8/10

Sleep

Baseline scores were similar for both groups, indicating a sample with poor sleep (PSQI: Intervention 13.4 [SD 2.6], Control 12.8 [SD 2.9]); reporting low TST (Intervention 6.1 [SD 0.6], Control 5.45 [SD 1.1]).

PSQI global scores showed a mean improvement for the intervention group of 6.6 (SD 3.3) (6 h 36 min) and control

Table 4 Adverse events recorded

Event	Study related (over the 8 weeks of the pilot RCT)				
	Unrelated	Unlikely	Possible	Probable	Definite
Musculoskeletal pain	CCCC			I I I I I I I I I I I I I I I I I I I[a]	
RA Flare-up	C C	I I			
Nausea	C	I			
Cold/Flu	C I				
Chest infection	C I				
Fall	C C[b] I I[c]				

I Intervention (10/10), *C* Control (8/10), *RA* rheumatoid arthritis

[a]5 from 1 participant

[b]2 from 1 participant

[c]2 from 1 participant

0.25 (SD 1.1) (15 min), while TST showed a mean improvement for the intervention group of 1.65 (SD 0.39) (1 h 39 min) hours and control 0.56 (SD 0.46) (34 min) (Table 6).

PSQI subcomponent for 'Sleep Latency' indicates an improvement for the Intervention group of 16 min (SD 17.2), compared to 3 min (SD 22.0) for Control, while PSQI subcomponent 'Sleep efficiency' improved 12.5% (SD 8.3) for the Intervention group compared to 5% (SD 7.1) for Control.

PSQI subcomponent 'Sleep quality' indicated those in the intervention improved their sleep quality from very bad/fairly bad to fairly good/very good, while those in control reported no change at very bad/fairly bad.

Pain (RA)

Mean reduction (VAS 0/10) for intervention of -1.9 (SD 1.2) compared to 0.4 (SD 0.8) for control.

Mood

Moderate depression (QIDS-SR: Intervention 11.7 [SD 3.9], Control 12.2 [SD 3.3]), and moderate to high for both state anxiety (STAI-State: Intervention 47.3 [SD 2.2], Control 45.4 [SD 3.9]) and trait anxiety (STAI-Trait: Intervention 42.6 [SD 3.0], Control 45.5 [SD 3.9]).

Functional limitation

HAQ scores mean difference − 0.60 (SD 0.42) for intervention and 0.14 (SD 0.28) for control.

Fatigue

Reduced levels of fatigue for intervention − 11 (IQR − 16, − 7) compared to control 1 (IQR − 1, 3).

Barriers to exercise

The EBBS statement number 26, 'Exercise helps me sleep better at night', asks participants to indicate the degree to which they agree or disagree with the above statement. Pre-intervention 9/10 Intervention participants and 9/10 Control Disagreed/Strongly Disagreed; Post-intervention 10/10 Intervention participants Strongly Agreed/Agreed, and 8/10 Control Disagreed/Strongly Disagreed with the above statement.

Discussion

The aim of this pilot RCT was to determine the feasibility of walking as an exercise intervention in RA management for improving sleep (time, quality and disturbance), and to examine if a larger adequately powered trial would be indicated. The data from this study indicate that the walking-based intervention was both feasible and safe for people with RA who have poor sleep, moderate-to-severe disability and moderate disease activity. This study provides preliminary evidence that this approach to exercise could be a beneficial option in improving TST and sleep quality, thus a larger study powered to test for effect is warranted. Benefits of such a programme could extend beyond sleep to include increased self-efficacy, improved pain, stiffness, and physical function.

Identifying participants at two rheumatology clinics resulted in 60% ($N=24$) of the targeted sample size ($N=40$) being achieved within a three-month recruitment period, indicating an interest among people with RA trialling walking for the management of poor sleep. A commonly reported issue with the conduct of RCTs is that recruitment is often slower or more difficult than expected [58]. There are promising strategies for increasing recruitment to trials, most notably telephone reminders, open-trial designs with focus

Table 5 Statistics for secondary outcomes

Outcome	Intervention (number: SD)			Control (number: SD)		
	Week 0	Week 9	Mean difference[a]	Week 0	Week 9[b]	Mean difference[a, b]
MVPA (minutes)						
Median (IQR)	152 (93, 211)[b]	287 (219, 355)	134 (70, 197)	115 (83, 148)	130 (97, 165)[c]	17 (− 4, 39)
95% CI	36–236	100–405	44–253	45–199	98–201	− 11 to 56
PSQI (0/21)						
Mean (SD)	13.4 (2.6)	6.8 (1.4)	− 6.6 (3.5)	12.8 (2.9)	13.5 (2.9)	− 0.25 (1.2)
95% CI	11.9, 15	6.0, 7.7	− 8.9, − 4.6	10.8, 14.7	11.5, 15.3	− 1.0, 0.60
Sleep duration (TST)						
Mean (SD)	6.10 (0.6)	7.75 (0.4)	1.65 (0.4)	5.45 (1.1)	5.63 (0.95)	0.56 (0.49)
95% CI	5.80, 6.40	7.55, 7.94	1.39, 1.90	4.80, 6.10	5.00, 6.25	0.25, 0.92
Pain VAS (0/10)						
Mean (SD)	5.3 (1.8)	3.4 (1.4)	− 1.9 (1.2)	4.6 (2.1)	5.2 (2.2)	0.4 (0.8)
95% CI	4.2, 6.4	2.6, 4.2	− 2.7, − 1.2	3.3, 5.9	3.6, 6.7	− 0.1, 0.9
POMS (− 46/200)						
Mean (SD)	45.2 (30.1)	− 10.5 (7.1)	55.7 (29.6)	45.7 (31.3)	49.9 (38.3)	1.1 (19.7)
95% CI	28.4, 64.1	− 14.9, − 6.2	38.4, 73.4	27.6, 64.1	26.4, 77.4	− 12.7, 14.0
QIDS-SR (0/27)						
Mean (SD)	11.7 (3.9)	4.3 (1.6)	− 7.4 (3.4)	12.2 (3.3)	11.9 (3.4)	0 (3.2)
95% CI	9.5, 14.3	3.4, 5.3	− 9.5, − 5.3	10.1, 14.1	9.4, 14.2	− 2.1, 2.1
STAI-State (0/80)						
Mean (SD)	47.3 (2.2)	46 (4.1)	− 1.3 (4.2)	45.4 (3.9)	47.0 (5.8)	1.7 (4.0)
95% CI	45.7, 48.9	43.1, 48.9	− 4.3, 1.7	45.3, 45.5	42.1, 51.9	− 1.7, 5.0
STAI-Trait (0/80)						
Mean (SD)	42.6 (3.0)	42.1 (3.7)	− 1.1 (4.9)	45.5 (3.3)	44.8 (4.1)	− 0.3 (3.7)
95% CI	40.4, 44.8	39.5, 44.7	− 4.6, 2.4	42.7, 48.2	41.3, 48.2	− 3.4, 2.9
CDAI (0/76)						
Mean (SD)	16.7 (5.4)	10.0 (6.5)	− 0.7 (3.6)	15.7 (4.6)	16.8 (3.9)	0.69 (2.87
95% CI	13.7, 20.2	6.8, 14.9	− 9.0, − 4.6	13.2, 18.9	16.8 (3.9)	− 1.2, 2.6
HAQ (0/3)						
Mean (SD)	1.5 (0.6)	0.9 (0.5)	− 0.60 (0.42)	1.3 (0.7)	1.6 (0.6)	0.14 (0.28)
95% CI	1.0, 1.9	0.6, 1.2	− 0.8, − 0.3	0.9, 1.8	0.3, 0.9	− 0.03, 0.4
EQ-5D™-3 L VAS (0/100)						
Mean (SD)	60.4 (8.6)	70.7 (7.4)	10.4 (4.2)	59.8 (8.4)	60 (8.2)	0.3 (3.4)
95% CI	54.3, 66.5	65.4, 76.0	7.4, 13.4	53.8, 65.8	54.1, 65.9	− 2.1, 2.8
BRAF-MDQ (0/70)						
Median (IQR)	28 (19, 37)	17 (9, 25)	− 11 (− 16, − 7)	29 (18, 41)	32 (18, 45)	1 (− 1, 3)
Range	14–55	7–41	− 18 to 3	11–68	14–66	− 2 to 4
EBBS (0/172)						
Mean (SD)	114.1 (7.9)	121.2 (7.3)	7.1 (6.1)	112.5 (8.8)	114.2 (11.4)	0.38 (3.62)
95% CI	108.4, 119.8	115.9, 126.5	2.7, 11.5	106.2, 118.8	104.7, 123.8	− 3.1, 3.8
Estimated $V0_2$max (ml/kg/min)						
Mean (SD)	27.4 (5.4)[b]	39.5 (3.4)[b]	13.4 (6.0)	30.1 (4.5)	31.3 (6.8)[c]	0.1 (4.2)
95% CI	22.9, 31.9	36.7, 42.4	8.4, 18.35	26.9, 33.3	25.1, 37.6	− 3.7, 4

PSQI Pittsburgh Sleep Quality Index, *TST* Total Sleep Time, *VAS* Visual Analogue Scale, *POMS* Profile of Mood States, *QIDS* Quick Inventory of Depressive Symptomology (Self-Report), *STAI* Self-Evaluation Questionnaire, *CDAI* Clinical Disease Activity Index, *HAQ* Health Assessment Questionnaire, *EQ-5D-3L* EuroQol EQ-5D-3 L, *BRAF* Bristol Rheumatoid Fatigue Multidimensional Questionnaire, *EBBS* Exercise Benefits/Barriers Scale, *MVPA* Moderate to vigorous physical activity, *Modified BRUCE* VMO2 scale

[a]Difference in group means between baseline and primary time point

[b]Data available for 8/10

[c]Data available for 7/10

Table 6 PSQI selected subcomponents

PSQI	Intervention			Control		
Selected sub-scales	Week 0	Week 9	Change	Week 0	Week 9	Change
Sleep duration (h), mean ± SD	6.10 (0.6)	7.75 (0.4)	1.65 (0.4)	5.45 (1.1)	5.63 (0.95)	0.56 (0.49)
Sleep latency (mins), mean ± SD	32 (19.4)	16 (12.8)	− 16 (17.2)	30 (26)	27 (14)	− 3 (22)
Sleep efficiency (SE) (%), mean ± SD	66.5 (9.7)	79.0 (10.7)	12.5 (8.3)	67.5 (8.0)	72.5 (9.2)	5 (7.1)
Sleep quality (number)						
Very bad	4	0	− 4	5	5	0
Fairly bad	5	0	− 5	5	5	0
Fairly good	1	9	8	0	0	0
Very good	0	1	1	0	0	0
Sleep medication (prescribed or 'over the counter') (number)						
Not during the past month	5	6	1	5	5	0
Less than once a week	0	1	1	0	0	0
Once or twice a week	2	1	− 1	1	2	1
Three or more times a week	3	2	− 1	4	3	− 1

PSQI Pittsburgh Sleep Quality Index

groups to investigate methods to improve the recruitment of males would be recommended. There is also evidence to indicate that recruitment in September, is more beneficial with potential increased interest from participants [59].

An excellent retention of participants from both groups was achieved, indicating satisfaction and acceptability. High PSQI scores from the participants were consistent with other studies in patients with chronic pain [60], therefore, the PSQI would be a useful screening tool for future trials. Further refinement of the inclusion criteria using a cut-off point from the PSQI of ≥ 5 would ensure a greater homogeneity of the sample and only recruit those with significant RA-related poor sleep quality. Sleep efficiency (SE) ranged from 66.5% pre-intervention to 79% post-intervention, which is considered below normative limits ≥ 85%. It is acknowledged that self-reported sleep may have conflicting reports from participants' recall of their sleep quality, which highlights the need to collect objective data in a future RCT. Although polysomnography (PSG) is the gold standard sleep assessment method, it is expensive and time-consuming, therefore, actigraphy might be a more appropriate method. Advances in the availability of smartphone apps and wearables for health monitoring is staring to provide a previously unobtainable mechanism to collect regular self-reported symptoms and objective sleep data, while embedding data collection into participants' everyday lives e.g. a triaxial accelerometer MotionWatch8 [61]. However, it is important to note that quiet wakefulness is categorized as sleep by some actigraphy methods, thus highlighting the need to continue to use both subjective and objective outcome measures in a future RCT.

From the NSF sleep diary, it was possible to obtain TST, SOL, and SE for each participant on a nightly basis during the intervention. However, due to issues with compliance in completing the diary, there were many missing values in these data and as a result the data could not be analysed. Therefore, the poor compliance with the sleep diary over a 7-night period, as recommended by the NSF and the American Academy of Sleep Medicine (AASM) [6] needs to be addressed. Recent developments in phone and tablet technology that can integrate an electronic diary application, with automatic prompts for those not responding or forgetting, present alternatives to improve the rate of completion of sleep diaries.

Although there is a growing consensus that exercise will benefit sleep for those experiencing a chronic health disorder, research is still inadequate for those with a rheumatic condition [5, 14, 62]. Because of the multifactorial nature of RA, that is, how it affects a person both physically and psychosocially, engaging in exercise may not only improve sleep quality but also mitigate some of its symptoms [8, 17]. As exercise prescription is a core skill for some health professionals (HPs) [16], they should, therefore, play an important role in educating people with RA on the benefit of increasing their exercise levels in improving their TST and sleep quality. Given that a recent systematic review has provided further evidence that being physically active is an important contributor to symptom management in people with RA [63], it is essential that any negative beliefs regarding exercise's impact on sleep are challenged by HPs when seeking to promote their exercise levels.

Comprehensive reporting of adverse events (AEs) indicated that the current study was low risk for individuals with RA, with no serious AEs attributed to the study. The most common AE associated with the intervention was delayed onset of musculoskeletal soreness (DOMS), lasting 24–48 h after class, due to previous inactivity. The risk of falling was

not part of this study and as the adverse events were low the intervention is not deemed to increase the risk of falling. However, the risk of falling is an important area of research that still has to be fully explored in people with RA. In any future, fully powered RCT to assessing participants for their risk of falls should be considered.

Sleep has an essential role to play in our immune system and is necessary in the restoration and maintenance of homeostasis [7]. Sleep disorders may trigger immune system abnormalities inducing autoantibody production, which may lead to the development of autoimmune disease such as RA [7]. People with RA have varied sleep patterns and from our study have reduced TST, in addition to having lower physical activity and exercise profiles. The results presented from our pilot RCT will contribute data to the field of exercise and sleep which is currently lacking [64].

Study strengths and limitations

This study presents preliminary evidence that a walking-based exercise intervention has a positive impact on sleep in people with RA. However, exercise, is not, by itself, enough evidence that it is the primary impact, therefore, as sleep is a complex issue it may require several lifestyle changes to improve same.

This was a rigorous and controlled, single-blinded intervention conducted at a University research centre, with no dropouts from the Intervention group and all data analysed. The study indicates that the intervention is feasible, and that participant compliance with the exercise intervention and recording measures was high. However, as this study was a pilot RCT, it was not adequately powered to detect significant differences between the intervention and control group and may be of insufficient length to determine any impact on clinical outcomes. Results of statistical analysis should be interpreted with caution due to small sample size; however, preliminary results are encouraging. In addition, data on comorbidities and specific steroid medications were not collected in this study, but are recommended in any future RCT.

A further limitation relates to the sample size of the study. Recruitment took place over the summer period due to the timeline of the study. A summer recruitment period was less than ideal and reduced the availability of potential participants due to the holiday season. Future research should consider recruitment in the Autumn.

Participants in this study were independently mobile and able to be active and, therefore, may not be representative of those with greater mobility limitations and with a variety of activity levels.

Involvement of public and patients in research is associated with improved outcomes and translation into practice and is advocated by the European League against Rheumatism (EULAR) recommendations through the inclusion of two patient representatives in scientific projects [65], which this study has facilitated. Aiming to improving TST and sleep quality through increasing exercise may be a health promotion strategy that is feasible and safe for this population. Therefore, the implications of this study provide a framework for larger intervention studies and based on these findings, a fully powered trial of walking as an exercise intervention is recommended, preceded by focus groups to investigate methods to improve the recruitment of males.

Conclusion

This pilot RCT explored the potential of a walking-based exercise intervention to improve sleep in people with RA, to inform the development of a fully powered trial. This intervention was found to be feasible and safe to study participants, with those participants in the exercise group reporting improvements in TST and sleep quality compared to the control group.

The consistent positive improvements in sleep outcomes observed provide preliminary evidence of the effect of a physiotherapist led walking intervention on sleep in a sample of people with RA. Participants expressed positive comments in relation to the intervention, including overall enjoyment of the exercise programme. These findings should inform the design for a future larger trial RCT of a walking-based exercise intervention for people with RA, to improve TST, sleep quality, and sleep disturbances. The poor compliance with the sleep diary and the lack of males being recruited are limitations that warrant further investigation, however.

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