**Exercises to improve function of the rheumatoid hand: a randomised controlled trial.**

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**Abstract**

*Background*

Disease modifying biologic agents and other medication regimens have substantially improved control of disease activity and joint damage in people with Rheumatoid Arthritis of the hand. Commensurate changes in function and quality of life are not always observed. Tailored hand exercises might provide additional improvements, but evidence is lacking. We estimated the effectiveness and cost-effectiveness of tailored hand exercises in addition to usual care over a 12 month period.

*Methods*

In this pragmatic, multi-centre, investigator blind parallel-group trial, we randomly assigned 490 adults with RA who had pain and dysfunction of the hands and had been on a stable medication regime for at least three months, to either usual care or usual care plus a tailored strengthening and stretching hand exercise programme. Treatments were delivered by physiotherapists or occupational therapists. The primary outcome was the Michigan Hand Outcomes Questionnaire overall hand function score at 12 months. The trial is registered as ISRCTN 89936343.

*Findings*

The two intervention groups had similar characteristics at baseline; 89% (438/490) provided 12 month follow-up data. In intention to treat analysis, improvements in overall hand function were 3.6 (95% CI 1.5 to 5.7) and 7.9 (95% CI 6.0 to 9.9) points in the usual care and exercise group respectively (mean difference between groups 4.4 (95% CI 1.6 to 7.1)). Pain, medication regimes and health care resource use remained stable over 12 months, with no difference between the groups. There were no serious or adverse events related to the treatment. The cost of tailored hand exercise was £156 per person; cost per Quality Adjusted Life Year was £9549 using the EQ-5D (£17,941 with imputation for missing data).

*Interpretation*

We have shown that a tailored hand exercise programme is a worthwhile, low cost intervention to provide as an adjunct to a range of medication regimens.

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**Introduction**

Rheumatoid Arthritis (RA) has a substantial impact on quality of life, function and productivity of millions of people across the world. The major effects of RA are on the synovial joints, particularly the hands.1 Best practice mandates aggressive control of joint inflammation with disease modifying drugs (DMARDS) and more recently, biologic agents. These medications have delivered substantial improvements in disease activity and minimised structural damage.2, 3 However, commensurate changes in disability, health related quality of life and deformity are not always observed.4, 5

Hand exercises may potentially enhance the impact of a range of medication regimens in hand RA, but evidence is lacking. If effective, exercise interventions are potentially low cost in comparison to other RA treatments, but rely on good compliance.6, 7 Evidence from small randomised controlled trials provides some proof of concept that exercise can restore or maintain function8 but larger trials with longer follow up are needed.

The aim of the Strengthening and Stretching for Rheumatoid Arthritis of the Hand Trial (SARAH) was to estimate, for people controlled on a range of medication regimens, the effectiveness and cost-effectiveness of adding an individually tailored, progressive exercise programme for the hands and upper limbs in addition to best practice usual care.

**Methods**

*Design*

The SARAH trial was a pragmatic, multi-centre, investigator blind, parallel group randomised controlled trial. A detailed protocol is published elsewhere.9

*Participants*

The setting was 17 National Health Service hospital trusts in England. Inclusion criteria were adults (≥18 years) with RA meeting the American College of Rheumatology clinical and immunological criteria,10 who reported active pain and dysfunction of hands, who were either not on a DMARD regime, or who had been on a stable DMARD regimen (including biologic agents if used) for three months or more. Exclusion criteria were upper limb surgery or fracture in the previous six months, pregnancy or waiting for upper limb surgery.

*Randomisation and masking*

We used a central telephone randomisation service at the Warwick Clinical Trials Unit. The study was individually randomised, with stratification by centre using a variable (random) block length of between 2 and 8. Allocation was computer-generated and revealed once the participant was registered into the trial. It was not possible to mask participants and therapists to treatment allocation. The outcome assessors were independent of intervention delivery and masked to group allocation. Participants were asked not to reveal allocation to the assessors at follow-up. We asked outcome assessors if they could guess the allocation of participants at the end of each assessment.

The first centre to commence recruitment was the University Hospitals Coventry and Warwickshire which started on October 2009, followed by South Warwickshire NHS trust, Basingstoke & North Hampshire Hospital NHS trust, Wrightington, Wigan & Leigh NHS Trust, Royal National Hospital for Rheumatic Diseases NHS trust, Winchester Eastleigh Healthcare NHS Trust, Poole Hospital NHS trust, Portsmouth Hospitals NHS Trust, Royal Bournemouth & Christchurch Hospitals NHS Trust, Dorset primary care trust, Worcestershire Acute Hospitals NHS trust, Nuffield Orthopaedic Centre NHS trust, George Eliot NHS trust, Heart of England NHS trust, Sussex community NHS trust, University Hospitals of Leicester NHS trust, Derby Hospitals NHS trust. Stratified randomisation meant that the arms of the trial were parallel; we accumulated participants in both arms from initiation of recruitment.

*Procedures*

We asked clinicians to identify potentially eligible patients during clinic visits or from clinic records and to provide a written invitation and information sheet. If willing, patients attended a face to face appointment with a research clinician to discuss the trial, check eligibility, complete baseline assessments and study registration. Patients were asked to give written informed consent according to principles of Good Clinical Practice and the Declaration of Helsinki.

*Interventions*

We have published a detailed description of the interventions elsewhere.11 Usual care was based on international clinical guidance and included joint protection education and, where indicated, functional splinting.12, 13 A maximum of three sessions of outpatient therapy were permitted, to a maximum of 1.5 hours contact time. Participants were provided with information sheets published by Arthritis Research UK and encouraged to remain active.

We added the exercise programme to usual care, and intended the exercises to be carried out daily at home for a minimum of 12 weeks. The programme included six sessions of face to face contact with a physiotherapist or occupational therapist. There were seven mobility exercises and four strength/endurance exercises against resistance provided by bands, balls or therapeutic putty. Participants had an initial assessment to tailor the exercise prescription to their strength, pain and flexibility. The initial intensity of exercise was set at moderate to somewhat hard using a modified Borg Scale.14 We used a standardised protocol to progress or regress the exercises, aiming to increase both repetitions and resistance over time.11 We provided participants with an exercise booklet with pictures and instructions describing the exercises as well as the resistance materials required. We incorporated evidence-based strategies to promote uptake and adherence to the exercise programme, including an exercise contract, diary, patient-led goal setting and regular review of goals.15

Drug therapy and surgery continued in both arms of the trial as indicated by clinical need. Manual therapy, resting splints or electrotherapies were not permitted in either arm because of lack of evidence of their effect, or evidence of ineffectiveness.16

Therapists were trained to deliver both the experimental and control interventions. All therapists received four hours of training covering theoretical and practical application of both interventions, and two short update sessions during the trial. Therapists detailed the content of all treatment sessions in a standardised log book and clinical records. Each therapist received at least one quality control assessment per intervention type, and all records were reviewed to ascertain attendance and for documentary evidence of assessment, progression and/or regression of exercises.

We defined patient compliance with the intervention as attendance at all face to face sessions with the therapist. Participants kept a diary record of exercise completion.

*Outcome measurements*

A detailed description of measurements is in the published protocol.9 Follow-up data were collected at four and 12 months after randomisation at a face-to-face research clinic appointment, supplemented by postal questionnaire and telephone where participants were unable to attend. The primary outcome measure was the overall hand function subscale of the Michigan Hand Outcome Questionnaire (MHQ) at 12 months. (range 0-100; higher score indicates greater function).17 Secondary outcomes were other subscales of the MHQ including the activities of daily living, pain, work performance, satisfaction, aesthetics MHQ sub-scales and the summed MHQ score (range 0-100; higher score indicates better performance). We measured pain using the Troublesomeness questionnaire (range 0-20; higher score indicates greater pain)18, and self-reported global change, benefit/harm and treatment satisfaction questions. We collected physical performance measures including isometric pinch and grip strength, dexterity, hand and wrist range of motion and joint alignment.9 We measured self-efficacy using the Arthritis Self-efficacy scale (7 items; higher score indicates greater self-efficacy).19 A modified tender and swollen joint count of the hands and wrist (22 joints in total, according to Fuchs et al20) was used to evaluate changes in disease activity, along with Erythrocyte Sedimentation Rate (ESR) and C Reactive Protein (CRP) collected from patient records. Health-related quality of life (Short Form-1221 (range 0-100; higher scores indicate higher quality of life) and EuroQol EQ-5D22 (range 0-1)) were collected for the health economic analysis. Self-assessment of exercise compliance was collected using five item self-reported questionnaire. Serious adverse events (death, life threatening events, hospitalisation, medical intervention, disability) were classed as related, unrelated and possibly treatment related as were all adverse events reported by clinicians, researchers or participants.

*Sample size*

A previous efficacy study, using a similar outcome measure, reported a standardised mean difference (SMD) of 0.4 (moderate).23 For this larger, more pragmatic multi-center trial, a SMD of 0.3 in the primary outcome would be realistic and meaningful, and similar to worthwhile effects found in other pragmatic studies of RA.24 To show this difference with 80% power at the 5% significance level, we required data on a total of 352 participants (using SAS procedure GLMPOWER). Allowing for a 25% loss to follow-up, we sought to recruit at least 469 participants. The original sample size calculation did not include inflation for therapist effects, although we included evaluation for these effects in the final analysis.

*Statistical analysis*

The analysis was intention to treat. We estimated means, standard deviations and proportions to provide descriptive data for each group. Treatment effects were estimated using generalised linear modelling, adjusted for baseline score, age, sex and pre-randomisation drug regimens (no DMARD, single non-biologic DMARD, combination non-biologic DMARD or biologic DMARD). Therapist effects were estimated from a random effect nested within centre. Statistical tests of interaction were used to perform pre-specified subgroup analysis on baseline drug regimen (no DMARD, single non-biologic DMARD, combination non-biologic DMARD or biologic DMARD) and disease duration (<5 years or 5+years) as we believed these could most significantly influence response to the interventions. We used published score specific guidance for managing missing data17, 25 and investigated the effects of missing data using multiple imputation analysis. Complier-average causal effect analysis (CACE) was used to estimate the effects of patient compliance on the primary outcome.26 Analyses were performed using SAS V9.2 software (SAS Institute Inc., NC, USA). One interim review was planned at one year after start of recruitment. As expected at this time there was insufficient 12-month data to test the primary outcome hypothesis so any consideration of stopping the trial was based on consideration of treatment uptake at four months and adverse event reports only.

*Adverse events*

Adverse Drug Reactions/ Serious Adverse Events were recorded by therapists or research clinicians at follow-up appointments or by participants themselves. These were recorded on a specific Event Notification form and classified through discussions with local investigators and the trial lead. We requested as much information as possible from the participants, particularly about the potential attribution of the event.

*Cost data*

Intervention costs were estimated from individual patient attendance records, averaged across participants attending at least one treatment session and included equipment, therapist time and training costs. We collected data on use of health care resources at 4 and 12 months and applied published unit costs to these services. Quality Adjusted Life Years (QALYs) were estimated from EQ 5D and SF-6D data. The incremental cost per QALY gained was estimated using complete case analysis and also with multiple imputations for missing data, using recognised methods for economic analyses.28

*Ethical approval*

The trial was approved by the Oxford C Multi-center Research Ethics Committee (REC reference 08/H0606/47).

**Results**

Participant flow is shown in Figure 1. Between October 2009 and May 2011 we screened 1606 people, of whom 512 were potentially eligible and willing to be randomised. After exclusions at the formal eligibility check we randomised 244 participants to usual care and 246 to the tailored exercise programme. Two participants recruited to the usual care arm withdrew their consent for any data to be used. The majority of randomised participants were recruited from out-patient clinics (194/246 in the exercise and 199/242 in usual care arm).

Outcomes were obtained for 89% (438/488) of participants at 12 months; 25 participants withdrew from follow up during the trial, with a greater proportion of these in the exercise arm (17/246 versus 8/242) (Figure 1). Lost participants tended to be younger and male. There was slightly greater loss to follow up in the exercise arm. Data quality was good, with few missing data. 90 and 83% of responses were taken using face-to-face clinical assessment at 4 and 12 months respectively. Postal and telephone responses contributed a remaining 8 and 14% and 2 and 3% at 4 and 12 months respectively, with no difference between the arms of the trial.

In total there were 103 reports of serious adverse events but none were deemed treatment related (deaths (n=2 both usual care), life-threatening conditions (n=3; 1 in usual care and 2 in exercise arms), hospitalisations (n=10; 3 in usual care and 7 in exercise arms), requiring medical intervention (n=2; 1 in usual care and 1 in exercise arms), disability (n=86; 38 in usual care and 48 in exercise arms, all accounted for by flares of rheumatoid disease). There were two reports of transient exacerbation of upper limb pain in the exercise arm. . Outcome assessors were able to correctly guess allocation in 54% of cases (with 50% representing an equal chance) but this had no influence on the effect estimates.

The randomised groups were well matched in clinical and demographic characteristics (Table 1). Over 90% of participants were being treated with biologics or non-biologic DMARDs. Slightly more participants in the exercise arm were using a combination of non-biologic DMARDs prior to randomisation, and fewer used a single DMARD. The most common biologic DMARDs used were Adalimumab (n=42/104, 40% of participants on biologics) and Etanercept (n=34/104, 32%), whilst Methotrexate was the most commonly used non-biologic DMARD (used by 342/424, 81% participants either monotherapy or combination). Medications other than biologic or non-biologic DMARDs (such as analgesics or mild opiates) were prescribed for a small proportion of the participants (n=38/488, 8%).

Details of treatments received are in Table 2. Forty-eight therapists provided treatment. Treatment was initiated at a median of 20 (IQR 12 to 34) and 19 days after baseline assessment (IQR (13 to 33) for the exercise and usual care groups respectively. Treatments were well attended with nearly all participants (225/242, 93%) completing treatment in the usual care arm and the majority of participants (184/246 (75%)) attending all six sessions in the intervention arm. Participants in the exercise group reported greater compliance with daily or any exercise at four months, this difference narrowed at 12 months. Comparison of treatment attendance and content across the two trial arms indicated that therapists complied well with the protocol (Table 2 ). There were no significant therapist effects (ICC <0.0001).

Table 3 provides estimates of treatment effect for patient-reported outcomes. For the primary outcome at 12 months, the exercise group improved by 7.9 points (95% CI 6.0 to 9.9) and usual care by 3.6 points (95% CI 1.5 to 5.7). The difference between groups was 4.4 (95% confidence interval 1.6 to 7.1 effect size 0.3)). In the CACE analysis the between group difference in the primary outcome was larger, 5.2 [95% confidence interval 2.6 to 8.0]). Changes in the secondary outcomes mirrored these trends, with significant differences in MHQ of ADL, work, and satisfaction sub-scales, MHQ summed score and self-efficacy. There was no statistically significant deterioration in pain or aesthetics in either group over the 12 months, and no between group differences. Participant’s global ratings of change in their hands and/or wrists were better in the exercise arm at both 4 and 12 months, (p<0.0001, Wilcoxon test). 44.7% of exercise arm participants reported improvement compared with 20.8% in the usual care arm at 12 months. 80.9% of exercise arm participants reported improvement compared with 63.4% in the usual care arm at 12 months (p<0.0001, Wilcoxon test). Participant ratings of satisfaction with treatment also favoured the intervention group at both time points (p=0.0347 at 12 months, Wilcoxon test).

Table 4 provides estimates of treatment effect for impairment and disease activity outcomes. There were small but significant improvements in the number of tender and swollen joints in the exercise arm at 4 months but not 12 months, but no substantial difference between groups in CRP, ESR or MCP joint deformity. Hand muscle strength and dexterity were significantly better in the exercise group over or at the 12 month time point. Flexibility improved in both groups.

The cost of a full course of exercise therapy was £156 per participant. Allowing for other health care use during follow up, the mean cost was £103 (95% CI -£622 to £838) higher with intervention than usual care. QALY gains were 0.01 for the EQ5D (95% CI -0.03 to 0.05) and 0.02 (95% CI 0.01 to 0.04) for the SF6D. For complete case analysis the incremental cost per QALY gain was £9549 for the EQ-5D and £7440 for the SF-6D (£17,941 and £23,228 with multiple imputations respectively).

There were no statistically significant sub-group effects and no statistically significant interaction between treatment and medication (p=0.626), or duration of RA (p=0.482) (data shown in Table 5).

**Discussion**

We have shown that a tailored hand exercise programme is a worthwhile, low cost intervention to provide as an adjunct to a range of medication regimes. Maximising the benefits of biologic and DMARD regimes in terms of function, disability and health related quality of life should be an important treatment aim.

Our participants were representative of the population of people living with RA in the UK in terms of age and gender.12 Minority UK ethnic groups were, however, under-represented. We recruited people who were stable on a medication regime prior to exercises, recognising that patients can find exercises very difficult when experiencing pain and poor symptom control. However participants were not patients with burnt-out quiescent disease. Over half were requiring/receiving either combination DMARDs or biologics and demonstrated significant tenderness and joint swelling in the hands.

In comparison to a good quality usual care control intervention of joint protection advice and splinting, exercise resulted in a doubling of the treatment effect in important areas measured by the relevant MHQ subscales at 12 months (overall hand function, ADL function, work, and satisfaction) and confidence to self-manage symptoms. This was a pragmatic trial and we pre-specified a modest difference for the primary outcome (standardised difference 0.3 equating to a small to moderate effect29 ) and this was achieved without worsening of pain, aesthetics (deformity) or change in medication use. Compliance measured by treatment attendance was high, and compliance with home exercise appeared good, particularly during the first four months. Responses in impairment level measures were generally favourable, although not absolutely consistent. The most likely explanation is the variable presentation in impairments between participants and the individual tailoring of each programme.

The costs of the intervention were small in comparison to the annual cost of providing medication regimens. For example, in the UK the cost of biologic drugs for RA is £7000 - £10000 per patient per year.30 Within trial cost effectiveness analysis indicates that hand exercises are likely to be a cost-effective use of NHS resources, lying within or below the accepted thresholds of £20,000 to £30,000 per QALY that suggest a cost-effective alternative to usual care in the UK. We are likely to have underestimated cost-effectiveness as the analysis was limited to a one year time horizon.

Methodological limitations of this study are similar to many other rehabilitation trials that participant and clinician masking is impossible to achieve with exercise interventions. The sustained effect of the intervention at one year after randomisation and at least six months after completing face to face contact, suggests that the observations are not placebo or non-specific effects. Sensitivity analyses demonstrated that loss to follow up and un-masking is highly unlikely to have affected the results as the primary outcome was collected by questionnaire independently of any clinician or investigator involvement. The exception is the health economic analysis, where despite good follow up, multiple imputation indicates greater uncertainty, most likely due to the combination of a relatively small QALY gain and very wide variation in the costs of rheumatoid-related healthcare for individual patients.

Scrutiny of attendance and treatment logs as well as patient-reported health care use indicated that there was unlikely to be any contamination between the arms. Whilst we pre-specified sub-group analyses, the sample size of the study was not powered for these and the findings that disease duration and pre-randomisation medication regime have no significant influence on treatment effect should be interpreted with caution. Other possible criticisms are that we did not use the full ACR recommended core set of disease activity measures.31 We excluded two of the seven ACR criteria related to global rating of disease as they were not applicable to the intervention. We asked clinicians to use a pragmatic and inclusive approach to identifying participants but because of Data Protection Law, we have minimal data on people who declined to participate. Hence we cannot rule out selection biases. Recall bias is possible for some questionnaires, but should be equally distributed across arms. We made no adjustment for multiple hypothesis testing, choosing instead accepted methods of a pre-specified primary outcome. We accounted for potential confounders in the stratified randomisation, and through baseline co-variate adjustment. Centre was addressed through the randomisation method; baseline function, DMARD usage, age, sex and therapist were addressed in the pre-specified analyses; interactions with time since original diagnosis, type of referral, ESR and CRP were also examined.

In conclusion, an exercise regime for the hand and upper limb is effective in restoring and retaining hand function in RA, with associated positive impacts on activities of daily living, work, physical and emotional role over a 12 month follow up.

**Panel: Research in context**

*Systematic review*

We searched MEDLINE, EMBASE, CINAHL, AMED, Physiotherapy Evidence Database (PEDro), OTseeker, Web of Science and WHO International Clinical Trials Registry Platform from date of inception to December 2013 using search strings for condition, intervention, body area and to identify randomised trials.

We identified six randomised controlled trials  (378 participants) addressing hand exercises, and an additional trial investigating a general upper limb intervention  (108 participants).32 In addition, we identified a narrative  review8 including 4 randomized studies, all of which were identified in our searches.

At the outset of the SARAH trial there was uncertainty about the value of hand exercises. All of the studies reported positive effects on one or more impairments of muscle strength, range of motion and/or pain. The duration of follow up and methods of measurement were highly variable, making it difficult to draw conclusions.  Only one study reported effects on hand function and these were positive.

Quality of studies was generally poor with either unclear or high risk of bias in multiple aspects of the majority of studies. All studies apart from one were underpowered and with short term follow-up.

*Interpretation*

The SARAH trial contributes additional, high quality evidence from a large and methodologically robust trial to support the use of hand exercises in the management of people with Rheumatoid Arthritis affecting the hands.

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*Conflict of interest statement*

None of the authors declare any conflict of interest.

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**Figure Legends**

Figure 1. CONSORT Flow diagram

**Tables**

Table 1. Baseline characteristics

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |
|  |  | **Usual Care**  **(n= 242)** | **Exercise**  **(n= 246)** |  |  |
|  |  |  |  |  |  |
| Descriptors |  |  |  |  |  |
| Age (Years), Mean (SD)  Sex (% female) |  | 635 (11)  186 (76%) | 613(12)  188 (76%) |  |  |
| Ethnic Origin, n (%) |  |  |  |  |  |
| White  Indian  Pakistani  Mixed  Other |  | 235 (98)  2 (1)  1 (<1)  1 (<1)  1 (<1) | 238 (97)  3 (1)  -  3 (1)  2 (1) |  |  |
| In Employment, n (%) |  |  |  |  |  |
| Full time employed  Part-time employed  Self-employed |  | 22 (9)  30 (12)  10 (4) | 29 (12)  26 (11)  11 (5) |  |  |
| Right/Left hand dominant, n (%) |  |  |  |  |  |
| Right  Left |  | 215 (90)  23 (9) | 226 (92)  18 (7) |  |  |
| Years since RA diagnosis, estimated by participant |  |  |  |  |  |
| Median (IQR) |  | 10 (4,22) | 10 (4,21) |  |  |
| Baseline ESR |  |  |  |  |  |
| Median (IQR) |  | 16 (8,28) | 15 (7,28) |  |  |
| Baseline CRP |  |  |  |  |  |
| Median (IQR) |  | 6 (3,12) | 5 (3,12) |  |  |
| Medications1,n (%) |  |  |  |  |  |
| Biologic DMARD  Combination non-biologic DMARD  Single non-biologic DMARD  Other medications |  | 52 (22)  53 (22)  118 (49)  19 (8) | 51 (21)  72 (29)  103 (42)  19 (8) |  |  |
| MHQ, Mean (SD) |  |  |  |  |  |
| MHQ overall hand function both  MHQ activities of daily living both  MHQ work  MHQ pain  MHQ aesthetics both  MHQ satisfaction both  MHQ overall score |  | 521 (164)  541 (250)  484 (220)  514 (199)  586 (22.1)  435 (22.3)  509 (16.9) | 521 (152)  545 (245)  482 (220)  519 (219)  569 (220)  439 (197)  506 (164) |  |  |
| SF-12, Mean (SD) |  |  |  |  |  |
| SF-12 aggregate physical scale (PCS)  SF-12 aggregate mental scale (MCS) |  | 345 (9.5)  489 (110) | 338 (98)  481 (107) |  |  |
| Pain/Troublesomeness, Mean (SD) |  |  |  |  |  |
| Pain troublesomeness overall score  Confidence in performing tasks  overall score (self-efficacy) |  | 485 (215)  687 (191) | 460 (222)  670 (203) |  |  |
| Clinical Assessment, Mean (SD),N |  |  |  |  |  |
| MCP joint deformity in degrees  Active wrist ROM score in degrees†  Combined finger flexion in mm‡  Composite finger extension in mm†  Thumb opposition score†  Swollen joint count  Tender joint count  Dexterity: Nine-hole peg test in secs  Maximum full hand grip force in Newtons  Maximum pinch grip force in Newtons |  | 74 (94), 238  901 (317), 239  128 (161), 238  202 (255), 231  80 (21), 241  41 (48), 241  48 (51), 241  273 (94), 240  1303 (731), 240  391 (196), 237 | 68 (84), 245  880 (296), 245  130 (161), 245  213 (244), 244  82 (22), 246  42 (48), 246  50 (540), 246  272 (82), 246  1342 (833), 245  402 (211), 243 |  |  |

† Greater score = greater movement

‡ Lesser score = greater movement

Table 2. Details of the interventions provided in the usual care and exercise arms

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  |  |  |  |
|  | **Usual Care Exercise programme**  **n = 251 n = 246** | t |  |  |
|  |  |  |  |  |
| Treatments delivered |  |  |  |  |
| Median number of sessions (IQR)  Did not attend any sessions n (%)  Attended assessment session only n (%)\*  Partial completion of treatment n (%)  Full completion of treatment n (%)  Time from randomisation to last treatment (months)  Self-reported exercise (>= 1-2 sessions per week)  At 4 months  At 12 months | 1 (1,2) 6 (5,6)  7 (3%) 8 (3%)  135 (56%) 8 (3%)  10 (4%) 46 (19%)  225 (93%) 184 (75%)  11 (05 to 17) 32 (27 to 40)  137 (62%) 174 (81%)  123 (57%) 128 (62%) |  |  |  |
| Treatment session components |  |  |  |  |
| Provided joint protection advice, n (%)  Provided ARC booklets, n (%)  Provided functional splinting n (%)  Modified/reviewed functional splinting? n (%)  Helped patient complete exercise diary? n (%)  Helped patient complete Personal exercise guide? n (%)  Median number of exercises progressed n (IQR)  Ran through discharge advice? n (%)  Discussed continuing with exercise programme? n (%) | 224 (95) 220 (924)  220 (936) 222 (933)  103 (438) 98 (412)  81 (345) 111 (466)  N/A 223 (937)  N/A 201 (845)  N/A 8 (3,10)  N/A 169 (710)  N/A 169 (710) |  |  |  |
|  |  |  |  |  |

\*No follow-up sessions were attended (usual care were expected to have between 1 and 3 sessions)

Table 3. Estimates of effect in primary outcome and patient reported secondary outcome measures.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | |  | |  | |  | |  |
|  | | **Mean change from**  **Baseline (95% CI)**  **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**  **Usual Care Exercise programme** | | **Mean treatment difference**  **(95% CI)** | | **P value** | | **Number of participants confirmed** |
|  | |  | |  | |  | |  |
| MHQ Overall hand  function exercise | |  | |  | |  | |  |
| 4 Months  12 Months  CACE‡ at 12 months | | 404 (217 to 591) 873 (6·83 to 1064)  356 (145 to 568) 793 (598 to 988)  N/A N/A | | 471 (232 to 711)  428 (149 to 706)  523 (262 to 801) | | 00001  0·0028  00001 | | 449  438 |
| MHQ ADL (both hands) | |  | |  | |  | |  |
| 4 Months  12 Months | | 257 (-040 to 474) 786 (544 to 1028)  227 (-004 to 459) 589 (366 to 813) | | 566 (264 to 869)  348 (031 to 666) | | 00003  00321 | | 448  436 |
| MHQ Work |  | |  | |  | |  | |
| 4 Months  12 Months | | 527 (262 to 792) 612 (368 to 856)  3·11 (023 to 598) 812 (536 to 1087) | | 104 (-239 to 448)  462 (082 to 842) | | 05518  0·0175 | | 445  436 |
| MHQ satisfaction (both hands) | |  | |  | |  | |  |
| 4 Months  12 Months | | 666 (401 to 931) 959 (686 to 1232  706 (416 to 995) 1036 (753 to 1318) | | 361 (012 to 709)  338 (-037 to 713) | | 00430  00784 | | 445  436 |
| MHQ Pain † | |  | |  | |  | |  |
| 4 Months  12 Months | | -511 (-758 to -263) -760 (-994 to -526)  -601 (-874 to -329) -826 (-1083 to -570) | | -330 (-650 to -011)  -240 (-592 to 112) | | 00433  01814 | | 445  437 |
| MHQ aesthetics (both hands) | |  | |  | |  | |  |
| 4 Months  12 Months | | 284 (027 to 541) 352 (089 to 614)  3·37(042 to 633) 470 (181 to 759) | | 039 (-296 to 374)  101 (-270 to 472) | | 08209  05933 | | 442  437 |
| MHQ summed score | |  | |  | |  | |  |
| 4 Months  12 Months | | 434 (267 to 600) 728 (565 to 891)  422 (223 to 621) 759 (575 to 943) | | 317 (091 to 543)  321 (053 to 589) | | 00063  00195 | | 451  438 |
| SF 12 Mental Component Score (MCS) | |  | |  | |  | |  |
| 4 Months  12 Months | | 058 (-056 to 173) 046(-066 to 159)  041 (-089 to 171) 219 (075 to 363) | | -016 (-158 to 127)  1·59 (-006 to 323) | | 0·8299  00593 | | 443  423 |
| SF 12 Physical Component Score (PCS) | |  | |  | |  | |  |
| 4 Months  12 Months | | 091 (003 to 180333) 204 (101 to 308)  003 (-096 to 103) 119 (023 to 214) | | 118 (-011 to 246)  093 (-035 to 222) | | 00743  01555 | | 443  423 |
| EQ-5D Health state | |  | |  | |  | |  |
| 4 Months  12 Months | | 001 (-003 to 004) 004 (001 to 007)  002 (-001 to 006) 003 (000 to 006) | | 002 (-002 to 006)  000 (-003 to 004) | | 03813  08714 | | 448  434 |
| Troublesomeness | |  | |  | |  | |  |
| 4 Months  12 Months | | -464 (-723 to -205)- -544 (-791 to -297)  -454 (-735 to -173) -432 (-715 to -149) | | -270 (-591 to 050)  -161 (-521 to 199) | | 00993  03810 | | 439  423 |
| Self-efficacy | |  | |  | |  | |  |
| 4 Months  12 Months | | 204 (-010 to 419) 578 (340 to 817)  111 (-144 to 366) 519 (245 to 792) | | 338 (045 to 630)  321 (-019 to 662) | | 00244  00651 | | 442  422 |
|  | |  | |  | |  | |  |

‡CACE = Complier-average causal effect analysis

† Higher score = more pain

Table 4. Estimates of effect in physical performance and clinical secondary outcome measures

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  |  |  |  |
|  | **Mean change from**  **Baseline (95% CI)**  **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**  **Usual Care Exercise programme** | **Mean treatment difference**  **(95% CI)** | **P value** | **Number of**  **participants confirmed** |
|  |  |  |  |  |
| Full hand grip force (Newtons) |  |  |  |  |
| 4 Months  12 Months | 735(2·43 to 1228) 1555(1017 to 2093)  957(366 to 1548) 1577(1011 to 2142) | 929 (201 to 1657)  641 (-187 to 1470) | 00129  01303 | 400  355 |
| Pinch grip force (Newtons) |  |  |  |  |
| 4 Months  12 Months | 315(160 to 470) 492 (274 to 54)  235(063 to 406) 533 (299 to 768) | 157 (-059 to 373)  301 (013 to 588) | 01547  00411 | 396  351 |
| Active wrist ROM score (degrees) † |  |  |  |  |
| 4 Months  12 Months | 275 (063 to 487) 484 (265 to 702)  421 (173 to 668) 456 (213 to 700) | 158 (-125 to 441)  027 (-272 to 326) | 02750  08587 | 401  356 |
| Combined finger flexion  Finger (mm) ‡ |  |  |  |  |
| 4 Months  12 Months | -339 (-454 to -225) -445 (-582 to -307)  -320 (-451 to -189) -392(-548 to -236) | -093 (-243 to 058)  -064(-240 to 113) | 02281  04793 | 398  355 |
| Composite finger  extension (mm) † |  |  |  |  |
| 4 Months  12 Months | 145 (-017 to 307) 404 (198 to 609)  145 (-076 to 365) 481 (277 to 684) | 255 (005 to 504)  405 (113 to 696) | 00462  00068 | 390  346 |
| Thumb opposition score† |  |  |  |  |
| 4 Months  12 Months | 018 (000 to 035) 031 (013 to 050)  012 (-007 to 030) 016 (-004 to 037) | 013 (-010 to 037)  010 (-016 to 036) | 02725  04416 | 403  359 |
| Dexterity: Nine-hole peg test (secs) |  |  |  |  |
| 4 Months  12 Months | -074 (-150 to 0·03) -139 (-197 to -081)  -009(-092 to 074) -133(-186 to -080) | -064 (-153 to 026)  -119 (-215 to -023) | 01643  00156 | 403  358 |
| Swollen joint count (both hands) |  |  |  |  |
| 4 Months  12 Months | -012(-073 to 048) -105 (-158 to -053)  -102(-171 to -034) -113 (-169 to -056) | -087 (-150 to -023)  -007 (-074 to 061) | 00077  08844 | 405  360 |
| Tender joint count (both hands) |  |  |  |  |
| 4 Months  12 Months | -038 (-102 to 027) -127(-186 to -068)  -115 (-186 to -043) -096 (-169 to -023) | -103 (-177 to -029)  012 (-077 to 100) | 00069  07955 | 405  360 |
| MCP joint deformity (degrees) |  |  |  |  |
| 4 Months  12 Months | -059 (-132 to 015) -092 (-157 to -027)  -032 (-101 to 036) -070 (-141 to 001) | -066 (-153 to 021)  -056 (-150 to 037) | 01357  02369 | 398  355 |
| Erythrocyte Sedimentation Rate (ESR) [log transformation] |  |  |  |  |
| 4 Months  12 Months | -009 (-020 to 002) -004 (-015 to 007)  -010 (-023 to 003) -004 (-018 to 010) | -006 (-023 to 011)  -002 (-018 to 015) | 04864  08323 | 276  252 |
| C-Reactive Protein (CRP) [log transformation] |  |  |  |  |
| 4 Months  12 Months | -018 (-032 to -003) 004 (-011 to 019)  -012 (-029 to 005) -014 (-029 to 002) | 032 (008 to 055)  -003 ( -024 to 019) | 00093  08185 | 322  291 |

† Greater score = greater movement

‡ Lesser score = greater movement

Table 5. Estimates of treatment effect in pre-specified sub-group analyses at 12 months

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  |  |
|  | **Treatment effect (95% confidence interval)** | **Number of participants confirmed** | **p (interaction)** |
|  |  |  |  |
| Time since diagnosis |  |  |  |
| < 5 years  5+ years | -608 (022 to 1194)  -372 (021 to 722) | 115  276 | 04822 |
| Baseline medication regime |  |  |  |
| Biologic DMARD only  Combination non-biologic DMARD  Single non-biologic DMARD  No DMARD | 470 (-112 to 1052)  620 (-009 to 1249)  420 (010 to 850)-184 (-1204 to 837) | 92  114  199  33 | 06261 |

Following screening in rheumatology clinic or therapy review list potentially eligible and approached (n=1042)

Excluded (n=530)

 Declined to participate (n=530)

## Allocation

## Enrollment

Allocated to Usual Care Arm (n=244)

 Received allocated intervention (n=244)

 Did not receive allocated intervention (n=0)

 Withdrew consent for data to be used (n=2)

Did not attend (n=5)

Completed intervention (n=235)

Discontinued intervention (n=2)

 Reason unknown (n=2)

Allocated to Exercise Programme Arm (n=246)

 Received allocated intervention (n=246)

 Did not receive allocated intervention (n=0)

## Analysis

## 4 month Follow-Up

Excluded (n=22)

  Not meeting inclusion criteria (n=6)

  Declined to participate (n=10)

  Did not attend appointment (n=6)

Due (n=238)

Responders (n=222)

 Full (n=190)

 Postal (n=28)

 Telephone (n=4)

Lost to follow-up (n=16)

 Unable to contact (n=10)

 Withdrawal (n=4)

 Death (n=2)

Discontinued intervention (give reasons) (n= )

## 12 month Follow-Up

Due (n=237)

Responders (n=216)

 Full (n=174)

 Postal (n=33)

 Telephone (n=9)

Lost to follow-up (n=21)

 Unable to contact (n=13)

 Withdrawal (n=8)

 Death (n=0)

Discontinued intervention (give reasons) (n= )

Due (n=242)

Responders (n=228)

 Full (n=211)

 Postal (n=15)

 Telephone (n=2)

Lost to follow-up (n=14)

 Unable to contact (n=10)

 Withdrawal (n=4)

 Death (n=0)

Discontinued intervention (give reasons) (n= )

Due (n=246)

Responders (n=224)

 Full (n=197)

 Postal (n=20)

 Telephone (n=7)

Lost to follow-up (n=22)

 Unable to contact (n=13)

 Withdrawal (n=9)

 Death (n=0)

Discontinued intervention (give reasons) (n= )

Withdrew prior to treatment (n=2)

Did not attend (n=6)

Completed intervention (n=184)

Discontinued intervention (n=54)

 Withdrew from treatment (n=46)

 Withdrew from trial (n=8)

## Treatment fidelity

Randomized (n=490)

Assessed at Research Clinic appointment (n=512)

**Fig.1. CONSORT Flow Diagram\_V2**