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The effects of arthritis gloves on people with Rheumatoid Arthritis or Inflammatory Arthritis with hand pain: a study protocol for a multi-centre randomised controlled trial (the A-GLOVES trial).

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Abstract

Background: Arthritis gloves are regularly provided as part of the management of people with rheumatoid arthritis (RA) and undifferentiated (early) inflammatory arthritis (IA). Usually made of nylon and elastane (i.e. Lycra®), these arthritis gloves apply pressure with the aims of relieving hand pain, stiffness and improving hand function. However, a systematic review identified little evidence supporting their use. We therefore designed a trial to compare the effectiveness of the commonest type of arthritis glove provided in the United Kingdom (Isotoner gloves) (intervention) with placebo (control) gloves (i.e. larger arthritis gloves providing similar warmth to the intervention gloves but minimal pressure only) in people with these conditions.

Methods: Participants aged 18 years and over with RA or IA and persistent hand pain will be recruited from National Health Service Trusts in the United Kingdom. Following consent, participants will complete a questionnaire booklet, then be randomly allocated to receive intervention or placebo arthritis gloves. Within three weeks, they will be fitted with the allocated gloves by clinical specialist rheumatology occupational therapists. Twelve weeks (i.e. the primary endpoint) after completing the baseline questionnaire, participants will complete a second questionnaire, including the same measures plus additional questions to explore adherence, benefits and problems with glove-wear. A sub-sample of participants from each group will be interviewed at the end of their participation to explore their views of the gloves received. The clinical effectiveness and cost-effectiveness of the intervention, compared to placebo gloves,

will be evaluated over 12 weeks. The primary outcome measure is hand pain during activity. Qualitative interviews will be thematically analysed.

Discussion: This study will evaluate the commonest type of arthritis glove (Isotoner) provided in the NHS (i.e. the intervention) compared to a placebo glove. The results will help occupational therapists, occupational therapy services and people with arthritis make informed choices as to the value of arthritis gloves. If effective, arthritis gloves should become more widely available in the NHS to help people with RA and IA manage hand symptoms and improve performance of daily activities, work and leisure. If not, services can determine whether to cease supplying these to reduce service costs.

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Background

Rheumatoid arthritis (RA) is a chronic inflammatory condition causing joint pain, swelling (synovitis), stiffness and muscle loss around affected joints [1]. It affects 1% of the population, and twice as many women as men. Peak onset is in the 40-60 age group, it is incurable and causes significant disability if untreated [2,3]. RA is managed with disease modifying anti-rheumatic drugs (DMARDs), rehabilitation and self-management education. People with persistent synovitis, where other pathologies are ruled out (i.e. undifferentiated inflammatory arthritis (IA), who do not yet meet the criteria for RA [4]), also require specialist care and DMARDs, and are thus treated as if they have RA [1]. Most people with IA and RA have symptoms in both hands, resulting in problems with everyday activities, work and leisure. Many experience frustration and distress because of hand pain, stiffness and disability. A third are work disabled within five years [1].

Arthritis gloves are commonly provided by Rheumatology occupational therapists to people with IA or RA. These are worn for pain relief during the day or night and to improve hand function during the day. We surveyed Rheumatology occupational therapists identifying that most provide arthritis gloves [5]. Provision varies considerably between occupational therapists but averages a third of the patients they see. The most common make of glove provided is the mid-finger Isotoner glove (i.e. finger tips exposed to aid hand function) and the next commonest are Jobskin and Norco oedema gloves [5,6]. Provision of gloves appears to have risen following a randomised controlled trial (RCT) demonstrating an alternative treatment (resting splints) was ineffective in early RA [7].

125 Arthritis gloves are usually made of nylon and elastane (i.e. Lycra®). They are thought
126 to impact on hand symptoms through providing compression (pressure) and/or
127 warmth. Some models apply both and others warmth only. Isotoner gloves,
128 containing 20% elastane, exert the highest pressure of those makes available, at 23-
129 32mmHg [8]. Other makes exert less as these contain less elastane (e.g. the Jobskin
130 classic oedema gloves exert 15-25mm Hg and contain 11% elastane [9]). When
131 properly fitted (to be a "snug fit"), the gloves apply controlled pressure to the hand
132 [10]. The pressure is thought to: (a) remove extracellular fluid, thus reducing pain,
133 stiffness and improving finger motion; and (b) increase blood flow and consequently
134 warmth, reducing pain [10,11]. The glove material also provides warmth, contributing
135 to pain relief. Makes of arthritis gloves, which specifically apply pressure, are termed
136 compression or oedema gloves. It is unclear what a therapeutic level of pressure is, as
137 this has not been identified through physiological studies. However, based on
138 pressure information from manufacturers, therapists consider this is between 15-
139 32mmHg. We also hypothesize that arthritis gloves provide tactile feedback to the
140 glove wearer reminding them to take more care of their hand joints. Potentially, all
141 models of glove (however much pressure and/or warmth they apply) may be acting
142 through this mechanism. This effect was hypothesized in a pilot clinical effectiveness
143 and efficacy trial of thumb splints [12].

144 Despite their widespread use, evidence for the effectiveness of arthritis gloves is
145 inconclusive. In a recent systematic review, we identified only four trials evaluating
146 arthritis gloves. Trials were small and results inconclusive [13]. We therefore
147 developed this randomized controlled trial to evaluate the effectiveness and cost-

effectiveness of the most commonly used arthritis glove (i.e. Isotoner) in people with RA or IA.

Feasibility study

We conducted a feasibility study among patients with IA or RA (n=39) in 10 Occupational Therapy departments in Northwest England evaluating mid-finger Isotoner gloves (as these are the commonest type provided and apply the highest pressure). During this study we standardised arthritis glove eligibility criteria, glove treatment protocols (including the arthritis glove patient information sheet) with participating therapists (North-West College of Occupational Therapy Specialist Section in Rheumatology: NWCOTSS-R arthritis glove protocol [14]. The results of the study are reported elsewhere [15].

Objectives

The primary objective is to assess whether there is a clinically important difference in self-reported dominant hand pain during daytime activity between participants with RA or IA receiving intervention gloves (Isotoner gloves) in addition to usual care compared to participants receiving placebo gloves (Jobskin classic oedema gloves fitted at least one size too big to ensure similar warmth is provided but minimal pressure only is applied), plus usual care.

The secondary objectives are to:

i. assess the effectiveness of intervention gloves, relative to placebo gloves on self-reported: non-dominant hand pain during activity; dominant and non-dominant nocturnal hand pain; hand pain during the day at rest; hand stiffness; hand joint swelling; and hand function.

ii. evaluate the cost-effectiveness of arthritis gloves compared with placebo gloves, taking into account the cost of the gloves and other healthcare resources used by participants

iii. explore participants' views of: the effects of arthritis (intervention) and placebo gloves on hand symptoms, function, and their daily lives; acceptability of glove wear; and how and when they prefer to use these.

Trial Design

The A-GLOVES trial is a pragmatic, patient-blinded, multi-centre, superiority randomised parallel group trial of intervention gloves compared to placebo gloves in people with RA or IA and persistent hand pain affecting their ability to do daily activities. Analysis will be on an intention-to-treat basis. Ethical approval for this study has been obtained from the North of Scotland Local Research Ethics Committee [15-NS-0077]. The study protocol was developed using the SPIRIT guidelines [16].

Methods

Study Setting

Study participants will be recruited from Rheumatology, Occupational Therapy and Hand Therapy departments in 23 hospitals across 17 NHS Trusts in England and Scotland in the United Kingdom (UK), as arthritis gloves are most commonly provided by rheumatology occupational therapists in secondary care.

Eligibility criteria

Inclusion criteria

Patients eligible for the trial must comply with all of the following at randomization:

1. Aged ≥18 years
2. Diagnosed with RA or IA by a Rheumatology Consultant
3. Have persistent pain in the proximal interphalangeal (PIPs) and/or metacarpophalangeal (MCP) joints causing either
   i) difficulty using their hands during the day (for day wear of gloves) or
   ii) disturbed sleep (for night wear of gloves) or
   iii) limited ability to use their hands when waking/ in the morning (for night wear of gloves)
4. Willing to wear arthritis gloves and participate in the trial
5. Able to read and understand English and,
6. Can provide informed consent

Exclusion criteria

People will be excluded from the study who have:

1. Been diagnosed with other rheumatic conditions, such as gout, psoriatic arthritis, ankylosing spondylitis, connective tissue disorders (systemic lupus, systemic sclerosis), resulting in inflammatory arthritis in the hand/s
2. Severe Raynaud's disease or other circulatory disturbances in the hand
3. Severe neuropathies (nerve damage) in the hand
4. Severe hand deformities
5. Any contraindications to wearing the gloves (e.g. eczema, infections, broken skin)
6. Previously worn arthritis gloves.

Interventions

Occupational Therapist Training in Glove Provision

Interventions will be delivered by 27 National Health Service (NHS) Rheumatology occupational therapists (≥Band 6 i.e. clinical specialists). Participating therapists must attend a one-day clinical trial training programme delivered by expert Rheumatology occupational therapists and the research team. This will include: trial background; key study procedures; and practice in providing the intervention and placebo gloves in a standardised manner. The A-GLOVES Occupational Therapy Glove Provision Manual, developed by the research team with the NW-COTSS-R, will be followed when fitting these gloves [17].

In addition to the training day, the Trial manager will conduct site visits to ensure all Principal Investigators, research facilitator/s (i.e. nurses/ other staff employed in the NHS to assist with recruitment into trials) and occupational therapists involved in the study understand how to explain the study and arthritis gloves appropriately, to ensure participants are not unblinded to the intervention.

Glove Fitting

The intervention group will receive correctly fitted mid-finger length Isotoner arthritis gloves. The placebo group will receive mid-finger length Jobskin classic oedema gloves fitted at least one size too large, to ensure they do not apply therapeutic levels of compression. When fitting gloves, the occupational therapist will measure participants' MCP circumference to determine the glove size required. Therapists will also use their clinical judgement to determine appropriate fit. Usually, patients requiring gloves receive these for both hands as their hand pain and/or swelling is bilateral. However, if patients have unilateral pain and/or swelling, they are provided with a glove only for the affected hand.

Additional Interventions

All participants (in both intervention and placebo groups) will receive a booklet about hand self-management: "Looking After Your Joints when you have arthritis" [18]. This booklet is widely provided in clinical practice. They will also receive an information sheet about hand exercises, based on the Strengthening And Stretching For

Rheumatoid Arthritis of the Hand (SARAH) trial hand exercise programme for RA [19,20]. During the 12 weeks, participants will only receive brief training in joint protection and hand exercises, and this will not use cognitive-behavioural approaches. Most departments do not normally offer behaviourally based joint protection and/or hand exercise programmes (or where these exist, such programmes usually have waiting lists), thus participants are not being disadvantaged.

Modifications

In some instances, a glove may not be fitted if enlarged PIP joints or finger deformity prevent this. For those participants with an MCP circumference greater than 23.5cm (or fingers/hands too large in other respects), no gloves will be fitted, as an appropriately large size is not available from manufacturers. If the participant cannot be fitted with gloves, they still remain in the trial, in line with "intention-to-treat."

Adherence

Recommendations for when to wear gloves will be based on individual needs; most, but not all, patients will be provided with gloves for both hands. Most people experience hand pain during the day and are recommended to wear gloves during activity. Those experiencing hand pain at night, which interferes with sleep, will also be recommended to wear gloves at night. Gloves are not recommended to be worn continually. All participants will receive written information about glove wear and

care, using the sample information sheet in the A-Gloves Occupational Therapy Glove Provision Manual [17].

To check for correct glove fit and any problems, occupational therapists will either: within two to four weeks of glove provision offer a review appointment (in person or by telephone); or ask the participant to get in contact if experiencing problems, if this is their normal departmental policy. At the review appointment, participants will be reminded about their glove wear regimen and the need to continue to wear the gloves until the 12-week follow-up questionnaire is completed. At the end of their trial participation, they will be contacted with further instructions about future glove wear.

Adherence to glove wear will be assessed in the 12-week follow-up questionnaires, by asking participants to describe their glove wear for right and left hand gloves. This will include, over the last four weeks, the: average time worn during the day and/or at night; and the average number of days per week gloves were worn. The participant will also be asked to state whether they have obtained arthritis gloves from elsewhere (if they did so, as it is possible for patients to purchase gloves in shops and on-line) and glove wear related to these (if applicable).

Concomitant care

Occupational therapists are asked not to provide resting, wrist, finger or thumb splints or any other occupational therapy interventions (apart from joint protection and hand exercises) to participants whilst they are in the trial (i.e. during their 12 weeks of participation). However, participants are permitted to attend Physiotherapy for lower

limb interventions if required. Data on participants' use of concomitant care is collected via the 12-week questionnaire.

Outcomes

The primary outcome measure is 'hand pain during moderate activity' which was considered the most important outcome by glove-users in our feasibility study. This is measured as hand pain in the dominant hand during the day, on a typical day, when doing moderate hand activities, e.g. housework, cooking, Do-It-Yourself, gardening. In our feasibility study, 2% of participants received one glove for their non-dominant hand only. It is therefore possible that the primary outcome cannot be collected in a small number of participants in this trial.

Secondary outcome measures are hand pain when resting and at night; stiffness; self-reported hand condition; hand function; disability; and resource use and costs to measure cost-effectiveness of glove provision (Table 1).

Participant timeline

Participants will complete a baseline questionnaire following consent and prior to the randomisation at week zero. Within three weeks of randomisation, an occupational therapy glove fitting appointment will be arranged to ensure there is sufficient length of time to wear the gloves prior to the 12-week follow-up. Two to four weeks after

glove fitting (dependent on each departments' usual practice), participants will attend an occupational therapy review appointment, either in person or by telephone, as per departmental policy. Participants will receive the follow-up questionnaire at 12-week following the date of baseline questionnaire completion. (See Figure 1 and 2).

Data collection

The baseline questionnaire includes: demographic factors i.e. age, gender, living situation, number of dependents living with them, and employment status; and condition specific factors, i.e. duration of their symptoms, time since diagnosis, current medication regimen and whether they have had a steroid injection/ started on oral steroids within the last six weeks.

Both the baseline and the 12-week follow-up questionnaire include:

The primary outcome:

[1] Hand pain: measured on a numeric rating scale (NRS) of hand pain in the dominant hand during the day when doing moderate hand activities. The anchor points are no pain (0) to severe pain (10). The pain NRS is a widely-used outcome measure in RA clinical trials. During development and psychometric testing of a patient-reported outcome measure, it was identified that participants had a strong preference for completing NRS over visual analogue scales. This study also identified test-retest reliability of pain (on movement and at rest) were between r_s = 0.70 to 0.72. The pain NRSs had significant

correlations ($p<0.001$) with SF36v2 Bodily Pain scales (r_s -0.69 to -0.77) [21] (Table 1).

And secondary outcomes including:

[2] Stiffness: measured through a) Patient self-reported duration of early morning stiffness affecting the hands (hours/minutes); b) 0-10 point numeric rating scale of hand stiffness (with anchor points of no (0) and severe (10) hand stiffness) - separately for the dominant and non-dominant hands.

[3] Self-reported hand condition: a five-point rating scale of very severe/ severe/ moderate /good/very good.

[4] Hand function: measured by the Measure of Activity Performance in the Hand (Map-HAND), which has been shown to be unidimensional and have good reliability and validity in a British RA population [22,23] and the Michigan Health Questionnaire (MHQ), which assesses for the right and left hands separately: physical status of the hand (movement, strength sensation: 5 items); daily activities performed with the hands/arms (5 right and left; 7 bilateral); impact of their condition on their normal activities (5 items); pain frequency, severity and impact (5 items); perceived appearance of their hands (4 items); satisfaction with hand abilities (6 items) and also has good reliability and validity [24,25].

[5] Disability: the Health Assessment Questionnaire (24 items of daily function) [26]

[6] Health-related quality of life (HRQoL) is measured using the standardised five-item EuroQoL, 3-level version (EQ-5D-3L) [27,28], which is recommended by

National Institute of Health and Clinical Excellence (NICE) for economic evaluations in clinical trials and has proven responsiveness, reliability, and validity in trials of interventions for RA [29,30]

The outcome measures within the baseline and 12-week questionnaire are also listed in Table 1.

Patient Interviews

At 14 weeks, participants (n = 10 to 15 from each group) will be purposively selected to participate in a semi-structured, face-to-face or telephone interview to investigate their views on: benefits or negative effects of glove wear (including when at work for those who are employed); glove appearance, quality, comfort, ease of applying; and willingness to buy gloves in future. Purposive sampling will be based on: 1:3 male to female ratio (as per the distribution of RA in population), and a range of ages, baseline hand pain (mild / moderate/ or severe) and 12-week self-reported levels of adherence with glove wear. The semi-structured interview schedule is outlined in Table 2.

All interviews will be audio recorded, transcribed verbatim and thematically analysed by three researchers to increase the validity of findings.

Sample size

This was calculated using data from the feasibility study. Minimal clinically important differences for pain scales in RA are estimated as 1.1 points on a 0-10 scale [31,32].

The mean change in hand pain score during activity (measured four weeks post-intervention) was -1.03 (SD 2.22). As the SD from the feasibility data might be an underestimate, the 80% upper one-sided confidence limit of the estimated SD, i.e. 2.48 was used. To identify a 1.1 point difference, SD = 2.48, p = 0.05 and 80% power, 80 participants are required per group. Allowing for a 20% attrition (i.e. non-return of 12 week questionnaire and a small number (up to 2%) not receiving a glove for their dominant hand (because they only require a glove for their non-dominant hand, and therefore not providing primary outcome data), we intend to recruit 205 participants.

Recruitment

At each participating site a Principal Investigator (PI) (senior occupational therapist/ consultant rheumatologist) will be identified, to be responsible for identification, recruitment, consent and provision of baseline questionnaires, along with adherence to the study and treatment protocols, following Good Clinical Practice Guidelines.

Members of the health care team and occupational therapists at participating sites will identify adult patients with RA or IA and persistent hand pain during the patients' Rheumatology, occupational therapy or hand therapy appointment. Either a research facilitator or occupational therapist will then screen patients for eligibility using the A-Gloves Trial Eligibility Screening Form. (See Figure 3 for recruitment procedure). All eligible patients will be provided with a study explanation and information pack. (See Additional File 1).

If a site is encountering difficulty screening sufficient numbers in clinics, then potential participants will be identified from medical or occupational therapy records by members of the health care team. The patient will then be mailed a Study Information Pack by the research facilitator or occupational therapist. (See Figure 4 for recruitment procedure).

At the screening stage, participants identified as having had a steroid injection or started oral steroids in the last six weeks, but who otherwise meet the inclusion criteria, will not be consented but will be re-screened six weeks after the date of steroid injection/ starting oral steroids to re-check trial eligibility. Steroids can reduce hand pain and thus would be a confounding factor in evaluating glove effectiveness. If at six weeks they are still eligible, they will be re-approached for consent.

Participants may receive a steroid injection or start oral steroids following consent. If this occurs between consent and glove fitting, the occupational therapist will identify this at the glove fitting appointment and defer glove fitting for six weeks from the date of injection/ steroid start. It is not anticipated that this will be a common event. If the participant starts steroids following glove provision and their hands are still symptomatic, they will be advised to continue glove wear as prescribed, as this is a pragmatic trial. If the patient reports that their hands are no longer causing them pain or discomfort they will be advised not to wear the gloves. However, they will remain in the trial and complete the 12-week questionnaire, as we will be conducting an intention to treat analysis.

Following consent, by the research facilitator or occupational therapist, participants will be provided with a baseline (i.e. 0 weeks) questionnaire to complete and return

in a Freepost envelope to the trial manager. On receipt of the completed questionnaire, the trial manager will enter their details into a web-based MACRO database (managed by Lancashire Clinical Trials Unit [CTU]) and request that the unblinded CTU staff perform the assignment of the intervention.

Assignment of intervention

Allocation and sequence generation

Participants will be randomly assigned to either the intervention or placebo glove group with a 1:1 allocation generated and delivered by 'Sealed Envelope,' an online, central randomisation service (www.sealedenvelope.com). The randomisation schedule will be stratified by whether or not the participant has had a change in or received new medication (specifically DMARDs or biologics) within the last three months, using permuted blocks of random sizes.

Concealment mechanism

The block sizes or schedule will not be disclosed to the trial manager, occupational therapists or research facilitators to ensure concealment. Randomisation will occur only once the trial manager confirms a participant's eligibility, consent and that they have completed the baseline questionnaire.

Implementation

Within three working days of notification by the trial manager, unblinded CTU staff will perform the randomisation and securely e-mail a referral for either intervention

or placebo gloves to the relevant site. Within three weeks of referral, the occupational therapist will make an appointment and provide the participant with the appropriate gloves.

Blinding

Due to the nature of the intervention it will not be possible for therapists to be blinded to group allocation. As most sites will only have one Rheumatology occupational therapist, both intervention and placebo gloves will commonly be provided by the same occupational therapist. During the glove training and site monitoring visits, the importance will be emphasised of not divulging to the participant whether they are receiving an intervention (arthritis glove) or a placebo glove. Therapists will be asked not to use the term "compression" glove (an alternative name for arthritis gloves in clinical practice) in any participant interaction, as this may unblind patients as to whether they are receiving an intervention or placebo glove. Participants will be kept blinded to group allocation by describing the study throughout as a comparison of two types of arthritis glove and not divulging the differences between these.

The trial manager will remain blinded to group allocation until the participant has completed and returned their 12-week questionnaire and the data been verified at the CTU. The trial manager will then be unblinded to group allocation for some participants in order to complete interviews with participants (n=24 to 30).

Data co-ordination and data entry staff at the CTU, responsible for baseline and 12 weeks questionnaires management, will be blinded to group allocation. However,

data entry for the Treatment Records (which identify the group allocation) will be conducted separately by the CTU Trial Management Team only, to avoid other CTU staff becoming unblinded. Statisticians and the health economist will be blinded to group allocation until analysis is complete.

Emergency unblinding

Not applicable as serious adverse events are not known to occur in clinical practice.

Data collection methods

Outcomes will be collected via self-reported questionnaires at baseline (i.e. prior to randomisation) and 12 weeks later. Glove provision will usually occur within three weeks of randomisation and referral to occupational therapy. Thus, at follow-up, most participants will have worn gloves for about nine weeks. Feedback from glove users indicates that they normally experience any benefits within a short-time of commencing glove-wear.

The trial manager (baseline) and CTU (12 weeks) will monitor return of all questionnaires and the quality of data.

- **At 1 week** after questionnaire provision/mailing, if the questionnaire is not yet returned, the trial manager [baseline questionnaire] or CTU [12-week questionnaire] will telephone /text / e-mail (as applicable) to remind the participant to return their questionnaire.
- **At 2 weeks** after questionnaire provision/mailing, if the questionnaire is not yet returned, the trial manager [baseline questionnaire] or CTU [12-week

questionnaire] will mail a reminder letter and a further copy of the relevant questionnaire (with Freepost envelope).

- **If the 12 week questionnaire is not returned by week 16,** the CTU will inform the trial manager who will then telephone the participant to obtain a minimal data set (i.e. at least dominant hand pain during moderate activity and if gloves are being worn (yes/no)). If possible, as much of the following will also be collected: dominant hand pain at night; hand stiffness; MAPHAND; hand condition severity scale; how their hands are in comparison to 12 weeks ago, i.e. before receiving gloves (much better/better/no change/ worse/ much worse). The trial manager will complete the minimal dataset on a 12-week questionnaire (with participant's PIN included), identifying on the front page that it is a minimal dataset completed by telephone. If the trial manager is unable to obtain this data, this will be recorded in the Trial Database and data entered as missing.

Data management

Data transfer from the University of Salford to CTU

The trial manager will ensure copies of all completed baseline and completed/corrected 12-week questionnaires are provided, in a timely and secure manner (e.g. copies of the questionnaires will be scanned and sent by e-mail using encrypted PDF), to the CTU for data entry. PDF scans of the questionnaires will be securely stored in password protected restricted access folders on the University of Central Lancashire network.

A written Data Management Plan (DMP), containing more detail about the Data Management procedures is available on request from the research team.

Baseline and 12 week questionnaires will be securely stored at the CTU following CTU procedures. At the end of the study, all electronic copies of participant questionnaires will be deleted and purged from the CTU network. Any paper questionnaires and documents (originals or copies) will be securely transferred to the University of Salford. Interview recordings will be deleted following transcription and analysis. Recordings and transcriptions will be stored on a secure server at the University of Salford. All data will be archived for three years in the Centre for Health Sciences Research, University of Salford. Quantitative data will become available to other researchers, on request, following completion and publication of the trial.

Statistical Methods

Primary effectiveness analyses will follow a pre-specified statistical analysis plan and will include the intention to treat (ITT) population. The primary analysis will use multiple linear regression to estimate the effect of group allocation on hand pain during activity, controlling for the stratification variable in the randomisation process (recent DMARD changes) and for the baseline value of the hand pain score. Secondary analysis will repeat the primary analysis method for all other outcomes, using appropriate modelling approaches (i.e. multiple linear regression, logistic regression or ordinal logistic regression, controlling for the stratification variable and the baseline value of the specific measure. Sensitivity analyses will assess for any potential bias in

the analysis of the primary outcome measure by excluding participants who were not given gloves, were given the wrong gloves, or who received steroids (oral or injection) between randomisation and outcome measurement (per protocol populations). Data will be analysed by person and using dominant hand results, as reported by the participant. No interim outcome analysis or sub group analysis will be undertaken. We will not undertake any data imputation for the primary analysis. We will undertake multiple imputation of the primary outcome as a sensitivity analysis. Questionnaire responses on medication use, other treatments, perceived benefit of gloves, continued glove use, adherence and occupational therapist treatment record data will be reported as numbers/proportions or means/SD, with 95% confidence intervals. Analyses will be undertaken in Stata version 14 or later [33].

Economic evaluation

The economic analysis will include costs to health and social care service providers and health benefits to patients. The time horizon for the evaluation is 12 weeks as per the scheduled trial follow-up. As such neither costs nor outcomes will be discounted. The data will be analysed on an intent-to-treat basis.

The measure of health benefit for the primary economic analysis will be quality adjusted life years (QALYs). This will be estimated from the EQ-5D-3L and associated utility tariffs. Secondary analysis will explore the cost-effectiveness of arthritis gloves using the primary clinical outcome measure, change in hand pain during moderate activity between baseline and follow-up. The direct costs of healthcare resources

used during the trial will be estimated by combining the level of use reported by participants with the unit cost specific to that resource. The unit costs will be derived from published national average unit cost data, the price year will be 2016. Total direct costs will also include the cost of the gloves. Regression analysis will be used to estimate the net total costs and economic benefits of the arthritis gloves compared to the placebo gloves, adjusting for baseline values and the stratification variable (recent DMARD changes).

Cost-effectiveness will be measured as an incremental cost-effectiveness ratio (ICER) for the arthritis gloves versus the placebo gloves. As recommended by NICE for health technology appraisals [34], cost-effectiveness acceptability analysis will be conducted. Non-parametric bootstrapping of the incremental costs and outcomes (estimated from the regression analysis) will be used to estimate the probability that arthritis gloves are cost-effective compared to placebo gloves.

Data Monitoring

The trial will not have a separate Data Monitoring Committee (DMC), as the safety risks associated with this study are very low. Consequently, there are no stopping rules for safety. The project will be overseen by a Trial Steering Committee (TSC), which will perform this function.

Harms

There is minimal risk or discomfort associated with the intervention (Isotoner) gloves. If a participant has increased hand swelling due to an exacerbation of their condition after glove provision, this can affect fit and potentially cause tingling or numbness. The verbal and written instructions provided during glove provision emphasise that the participant should: regularly check their hands; not wear the gloves continually; stop wearing the gloves if they experience any discomfort or pain or there is any redness or skin reaction; and contact the occupational therapist if they experience any problems.

Glove use will be modified or discontinued by the treating occupational therapist only if an adverse event related to glove wear causes concern. This may occur at the review appointment or if the participant contacts the occupational therapist with concerns. Adverse events caused by arthritis gloves have been identified in clinical practice and therapists modify the wear regimen as applicable. Adverse events and modifications include:

- Numbness; pins and needles; and/ or fingertips becoming discoloured (i.e. they go red, white or blue) during glove wear. This may be due to gloves being too tight. A larger glove may be fitted if this occurs.

- Allergic reaction or skin irritation can occasionally occur. Gloves are either left off for a time and re-tried or discontinued.

- Sleep disturbance at night. This can occur because the gloves feel hot or itchy. Participants are recommended to wear the gloves for part of the night or leave them off when necessary.

It is unlikely any harm will arise from participants wearing placebo gloves as most adverse events occur due to pressure effects.

Any adverse event considered by the occupational therapist to be resulting from glove wear, or any other minor problems related to glove wear, will be recorded by the occupational therapist on the A-Gloves Occupational Therapy Treatment Record Form at the review appointment and a copy returned to the CTU Data Manager.

Auditing

The trial manager will conduct at least one on-site monitoring visit per year over the course of the study to all clinical sites to educate, support and solve problems. The trial manager will provide the research facilitator/ principal investigator with a site file checklist prior to the visit and ask them to ensure the site file is up-to-date. The trial manager will check the completed checklist and site file at the visit. There will also be central monitoring, by the CTU and trial manager, of quality of source documentation, including consent form completion and adverse event reporting.

The Chief Investigator will permit study-related monitoring, audits and inspections by the Ethics Committee, lead R&D department, the University and any NHS Trust

Research Governance Managers requiring this. The study will be monitored in accordance with NHS and University Research Governance procedures. The Chief Investigator will ensure that any regulatory authority is given access to all study related documents and study related facilities. Principal investigators will be asked to audit their site files at the beginning and end of the study using a checklist provided by the University Research Centre and to allow study related monitoring, audits and inspections as above.

Composition roles and responsibilities of: the co-ordinating centres, TMG and TSC and Data Analysis Team: Management of the trial is joint between the Centre for Health Sciences Research, University of Salford (Hammond, Prior) and Lancashire Clinical Trials Unit (Sutton). Prof Hammond (Chief Investigator), Dr Prior (Trial Manager)) at the University of Salford, in conjunction with advice and support from Dr Sutton (Lead, Lancashire CTU) and other CTU staff, as appropriate, and Dr Cotterell (Statistician) will be responsible for: (i) writing the study protocol and any revisions, obtaining all study approvals and any amendments, preparation of study documentation, study planning, contributing to Trial Management Group and Trial Steering Committee meetings, producing interim and final reports to the funder and approving agencies (ethics committees, Trust R&D departments) (ii) Serious Adverse Event reporting (iii) Trial master file management and ensuring sites have site files, and content is monitored periodically (iv) Budget administration in conjunction with Salford Royal NHSFT (Research & Development) and University of Salford (Contracts Officer, Research and Innovation) (v) Advice for Principal Investigators, Research Facilitators and occupational therapists s (vi) Site initiation visits with Research

Facilitators/ occupational therapists/ Principal Investigators (vii) Organising occupational therapy training in glove provision and study procedures and day-to-day management of the project. The Trial Management Group (TMG) consists of AH (Chair) and the protocol contributors (listed in author contributions), and YH as the trial manager). The TMG will approve documentation, study protocol procedures, advise on ethics application, monitor trial progress by reviewing the trial progress reports, any problems arising, be advised of any Serious Adverse Events, review findings and plan dissemination. The TMG will meet at 6 monthly intervals and receive reports of trial progress. Teleconferences and ad-hoc meetings will be held during the study if issues arise require discussion. The Trial Steering Committee (TSC) consists of: Dr Peter Klimiuk, Consultant Rheumatologist, Pennine Musculoskeletal Partnership Ltd, Oldham (Chair); Cathy Ball, Research Clinical Specialist Hand Therapist, Kennedy Institute for Rheumatology, Oxford; Dr Michael Callaghan, Research Fellow, University of Manchester and Clinical Specialist Physiotherapist, Manchester Royal Infirmary; Mike Bradburn, Senior Medical Statistician, Sheffield Clinical Trials Unit, SCHARR, University of Sheffield. The TSC will meet three times and also act as the Data Monitoring Committee (DMC) and provide trial oversight and data monitoring. The TSC will meet to approve the protocol, advise on procedures and progress, data monitoring and review findings and monitor trial progress by reviewing trial progress reports. The project does not have a DMC, as the safety risks associated with this study are very low. The TSC will have access to the blinded data on completion of the analysis. No interim analyses are planned.

Protocol Amendments: Any subsequent modifications to the protocol which may impact on the conduct of the study, potential benefit of the patient or may affect patient safety (including changes of study objectives, study design, patient population, sample sizes, study procedures, or significant administrative aspects) will require a formal amendment to the protocol. Such amendment will be agreed by TMG and TSC members and approved by the approving NRES Ethics Committee prior to implementation and notified to the participating Trust R&D departments in accordance with local regulations.

Administrative changes of the protocol are minor corrections and/or clarifications that have no effect on the way the study is to be conducted. These administrative changes will be agreed upon by TMG members and documented in a Memorandum filed in the trial master file. The approving NRES Ethics Committee may be notified of administrative changes at the discretion of the TMG. Protocols and documents will be version controlled.

Dissemination

Findings will be submitted to rheumatology and health professional conferences and journals. A summary of findings will be provided to relevant health professional and arthritis patient organizations, requesting these are included in websites and newsletters. We will also produce guidelines, for both therapists and patients, on how to correctly fit and wear arthritis gloves, based on the A-GLOVES Trial Occupational Therapy Glove Provision Manual [17] and disseminate these as above.

Discussion

This protocol describes a definitive, pragmatic, patient-blinded, and multi-centre superiority randomised parallel group trial, which aims to determine the effectiveness and cost-effectiveness of the use of arthritis gloves for people with RA or IA with persistent hand pain. The results of this trial will inform the evidence base to support the prescription of arthritis gloves for people with RA or IA and hand pain. The results of this study will be published as soon as they become available.

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Participating Sites and Principal Investigators: We would like to thank occupational therapy and Rheumatology departments and the participating staff and occupational therapists at the Mid Cheshire NHS Trust (Nicky Walker(PI), Jan Coleclough, Helen Sawle), St Helens and Knowsley Hospital NHS Trust (Yvonne Hough (PI), Pennine MSK Partnership (Charlotte Pugh, Jill Firth (PI)), Southport and Ormskirk Hospital NHS Trust (Mary Dooley (PI)), Northumbria NHS Trust (Anne Boulton (PI)), Northern Devon Healthcare NHS Trust (Jo Harness (PI)), The Royal Wolverhampton Hospitals NHS Trust (Jill Spicer (PI), Christine Mate), NHS Greater Glasgow and Clyde (Katie MacAlarey (PI), Patricia Bisset), Northern Lincolnshire and Goole Hospital (Anne Bontoft (PI), Sandra Lyle), Sherwood Forest Hospitals NHS Trust (Rachael Murphy, Philip Avery, Charlotte Brooks: PI Prof David Walsh, Consultant Rheumatologist; Debbie Wilson, research nurse), Pennine Acute Hospitals NHS Trust (Aviva Richards (PI)), Staffordshire and Stoke-on-Trent Partnership NHS Trust (Carol Graham (PI), Leeds Teaching Hospitals NHS Trust (Christine Beck (PI), Kirstie Neat), NHS Borders (Nicki Grey (PI)), Sheffield

Teaching Hospitals NHS Foundation Trust (Dervil Dockrell (PI), Sarah Wilson) and Central Manchester University Hospitals NHS Foundation Trust (Janet Perkins (PI)) for participating in this trial.

We also thank Angela Jacklin (RegOT), who provided advice for the development of the Glove Provision Manual and who helped with training the occupational therapists in clinical aspects of this study. Furthermore, we would like to thank to the Lancashire Clinical Trials Unit for their support in the conduct of this study, specifically Malcolm Auton for his support and advice about data management processes in the earlier stages of the trial, Denise Forshaw for advice on trial procedures, Glen Holt for technical support, as well as Jane Fitzgerald and Rosemary Horan for administrative support; Josh Wood (research administrator, University of Salford for assistance with trial set-up); and also Barbara Birtwistle (patient research partner) for her invaluable advice during trial planning.

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Availability of data and material: following analyses, the dataset will be available to AH, YP, SC, CS, EC and the TSC. On publication the dataset can be accessed by contacting AH..

Authors' contributions: AH is the Chief Investigator. AH and YP conceived the study. AH, YP, CS, SC, EC initiated the study design. YH, WJ, JA, JF and T'ON advised on implementing the design. YH and WJ advised on implementing the training and treatment protocol. AH, YP, SC, CS, JF, JA, WJ and T'ON are grant holders. SC and CS provided expertise in statistical analysis and clinical trial design and SC is leading the primary statistical analysis. EC designed the economic analysis plan and will carry out the economic analysis. All authors contributed to refinement of the study protocol (version 5 Dated 22.02.2017) and approved the final manuscript.

Competing interests: The authors declare that they have no competing interests.

Consent for publication: Not applicable.

Ethics approval and consent to participate: Ethical approval was obtained from the REC [15-NS-0077] and the University of Salford, School of Health Sciences Ethics Committee [HSCR 15-94**]** prior to the start of this trial. One major amendment (related to inclusion of methods to promote retention) has been approved. Occupational therapists and research facilitators recruiting participants to this study have completed Good Clinical Practice (GCP) and informed consent training. Eligible participants will need to provide written, informed consent before any study procedures occur.

773 **Sponsor**

774 The University of Salford, The Crescent, Salford, M5 4WT - 0161 295 5000.

775

776 **Research ethics**

777 This study has obtained ethical approval from the North of Scotland REC [15-NS-0077]

778 Protocol dated 22.02.2017v5.

779

780

781 **Additional file 1:**

782 A-GLOVES: Testing Arthritis Gloves in Rheumatoid/Inflammatory Arthritis

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Table 1. Content of the Baseline and 12-week follow-up questionnaires

Concept	Measurement Method	Details	0-wks	12-wks
Demographic and Condition Information	Date of birth			
	Gender			
	Time since RA or IA symptom onset			
	Time since RA or IA diagnosis			
	Employment status			
	Marital status			
	Living status (alone; or with family/ significant others)			
	Medication regimen (i.e. what drugs do they take for their arthritis);			
	Whether received a steroid injection/ oral steroid in the last 6 weeks			
	Hand dominance (i.e. whether they consider this to be right, left or both).			
Primary outcome	Hand Pain during activity	0-10 (0=no pain/ 10= severe pain) point numeric rating scale of hand pain in the **dominant** hand during the **day** [21]		
Secondary outcomes	Hand Pain	0-10 (0=no pain/ 10= severe pain) a) during a typical day during activities in the last week in the non-dominant hand; b) when resting- separately for the dominant and non-dominant hands; and c) at night –separately for the dominant and non-dominant hands.		
	Stiffness	Measured separately for the dominant and non-dominant hands:		

Concept	Measurement Method	Details	0-wks	12-wks
		a) Patient self-reported duration of early morning stiffness affecting the hands (hours/minutes) b) 0-10 point numeric rating scale of hand stiffness (no (0) and severe (10) hand stiffness)		
	Self-reported hand condition	a five-point rating scale of very severe/ severe/ moderate /good/very good.		
Hand Function	The Measure of Activity Performance of the Hand (MAPHAND) [22,23] The Michigan Hand Outcomes Questionnaire (MHQ) [24,25]	a self-reported measure of 18 items of performing daily activities with the hands assesses right and left hands separately: physical status of the hand (movement, strength, sensation: 5 items); daily activities performed with the hands/arms (5 right and left; 7 bilateral); impact of their condition on their normal activities (5 items); pain frequency, severity and impact (5 items); perceived appearance of their hands (4 items); satisfaction with hand abilities (6 items)		
Disability Economic analysis	The Health Assessment Questionnaire [26] EQ5D-3L [27,28] Your use of NHS and social services Your use of hospital out-patient appointments	24 items of daily function 5-items Scale (Mobility; Self-care; Usual activities; Pain/Discomfort; Anxiety/ Depression a) Any <u>planned</u> hospital overnight stays in the last 3 months b) List of planned admissions a) Any <u>planned</u> hospital outpatient appointments lasting 4 hrs or less in the last 3 months b) If yes, department, speciality and number of appointments		

Concept	Measurement Method	Details	0-wks	12-wks
	Your use of day hospital appointments	a) Any day or hospital outpatient lasting more than 4 hrs but not overnight during the last 3 months b) If yes, department, speciality and number of appointments		
	Your use of accident and emergency services	a) Any A&E attendance in the last 3 months b) If yes, the number of visits did not lead to hospital admission c) Were admitted into a hospital as an in-patient from the A&E d) If yes, department, reason for admission, where and when admitted		
	Your use of primary and community based health services	a) Use of services such as GP, Practice nurse, Nurse, Counsellor in the last 3 months b) If yes, number if visits to each		
	Your use of primary and community based health services	a) Use of services such as OT, Physio, Care worker, Home help, Social worker, Other in the last 3 months b) If yes, number if visits to each		
Medication	Current medication for RA/ IA			
	Any steroid injection/ oral steroids started in the last 12 weeks	Yes/No		
	If yes, the date of the injection/ started taking oral steroids	DD/MM/YY		
Health Status	Your own health state today	Measured by a 0-100 vertical scale (0=worst imaginable state & 100= best imaginable health state)		
Additional outcomes	Any other upper limb occupational therapy or physiotherapy treatment received in the last 12 weeks	Type of treatment received		
	Whether purchased or obtained from elsewhere, any other "arthritis" gloves.	Yes/No		

Concept	Measurement Method	Details	0-wks	12-wks
	If yes, what type these were			
	How their hands are in comparison to 12 weeks ago, i.e. before receiving gloves	(much better/better/no change/ worse/ much worse)		
	Concurrent use of any resting, wrist, finger or thumb splints			
	Adherence to glove wear	During the day and at night for right/left hand gloves; average time worn at night/ during the day; average number of days per week gloves have been worn		
	Whether participants considered gloves provided any benefit	Yes/No		
	Whether they will continue to wear the gloves provided	Yes/No		
	If they considered the gloves of any benefit, what were these			
	Any problems encountered when wearing gloves	Freetext		

Table 2. A-GLOVES Semi-Structured Qualitative Interview Schedule

A-GLOVES Trial: Qualitative Semi-structured Interview Schedule	
Opening/ Main Question	
"Having worn the arthritis gloves for up to 12 weeks, could you tell me about any negative or positive effects these have had on your hand pain and hand problems?"	
The following prompts may be used to expand on the answers given:	
1	What effect did they have on your hand pain, hand stiffness and ability to use your hands?
2	Were there any particular activities you found they helped with? [For example: personal care; household activities; leisure/social activities; driving; work].
3	Were there any particular activities you found they did not help with? [For example: personal care; household activities; leisure/social activities; driving; work].
4	How did you find wearing them?
5	How was it to put them on and off your hands?
6	Was there anything about the gloves or their effects which you think helped/ hindered your hand pain and hand problems?
7	If they were helpful: when did you find them helpful to wear: either in the day or at night (or both)?
8	If they were not helpful: when did you find them unhelpful to wear: either in the day or at night (or both)?
9	For those employed: Have you used them at work? If yes, were they helpful? And in what ways? If not helpful, why was this?
10	Did you have any problems wearing the gloves?
11	What did you think of the gloves appearance?
12	What did you think of the quality of the gloves you were given?
13	How did you find cleaning them?
14	Would you consider buying them in the future?
15	Would you change anything about them to make it better for your use? (e.g. colour, texture, amount of pressure applied, size, length)

Figure titles:

Figure 1. A-GLOVES Trial: Flow of Participants

Figure 2: SPIRIT flowchart: Schedule of enrolment, interventions and assessments.

Figure 3. Recruitment and Consent Flowchart: Rheumatology Clinic/ Occupational Therapy

Figure 4. Recruitment Flowchart via Medical/OT Records / health care staff and Study Information pack mailed/provided to Patient

Figure 1. A-GLOVES Trial: Flow of Participants

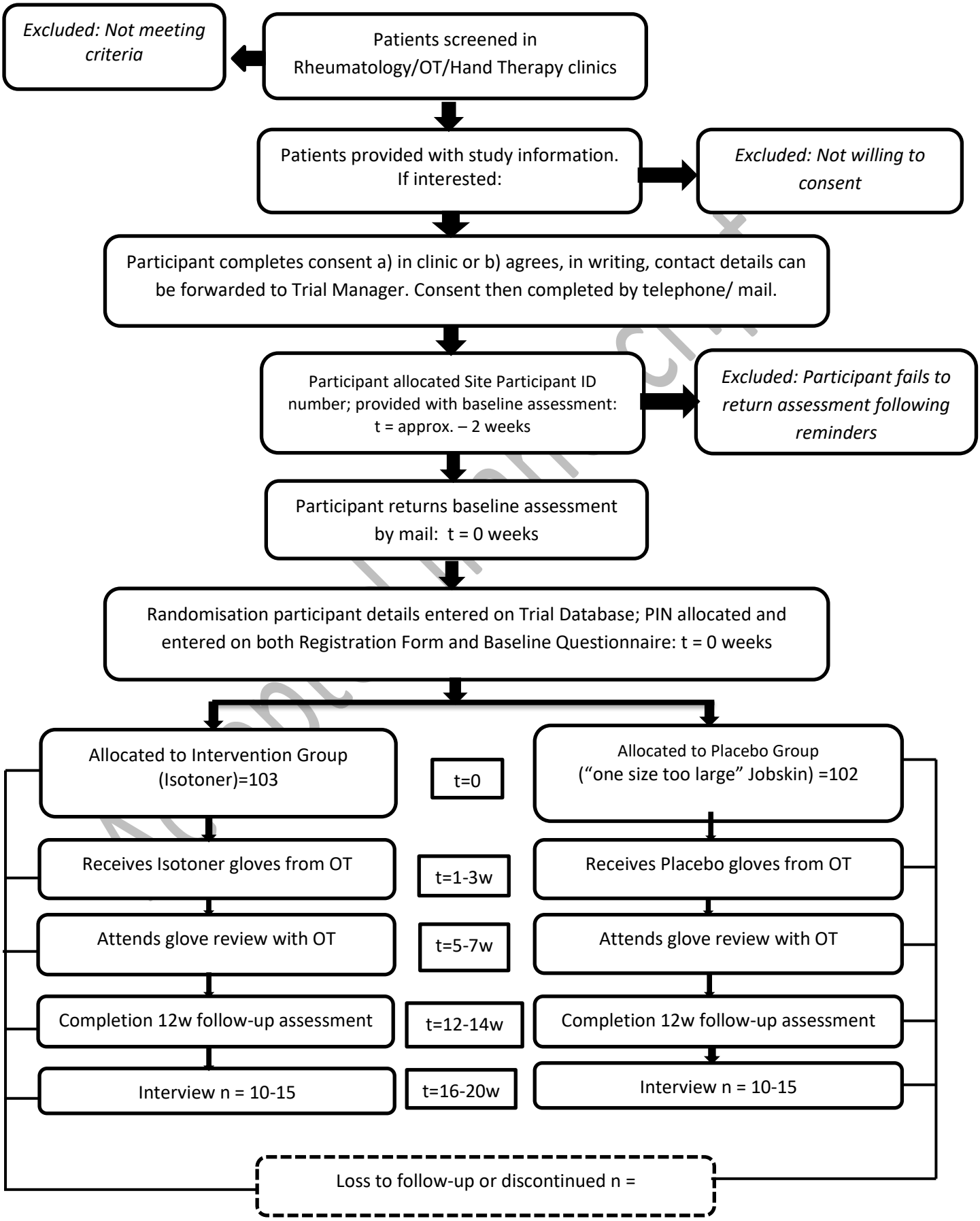


Figure 2: SPIRIT flowchart: Schedule of enrolment, interventions and assessments.

	Enrolment	Allocation	Post-Allocation		Close-out	Inter-view
TIMEPOINT	***-1 to 3 weeks; -21 to -1 days***	***0w Day 0***	***1-3w 4-21 days***	***4-7w 28-49 days***	***12w 84 days***	***16w 112 days***
ENROLMENT:						
Eligibility screen	X					
A-Glove Trial Contact Details	X					
Informed consent	X					
Registration form	X					
Baseline assessment given/mailed to patient	X					
Baseline assessment returned by patient		X				
Allocation		X				
INTERVENTIONS: (fitting and review appointments)						
Intervention Glove			X	X	→	
Placebo Glove			X	X	→	
ASSESSMENTS:						
Demographic data	X					
1: Hand pain during activity	X				X	
2: Hand pain rest/night;hand stiffness; hand function; disability; economic data	X				X	
Medication changes; other treatment; use other gloves; perceived change hand status; adherence; perceived benefits and continuing use					X	
OT Record Form Part 1 and 2			X	X		

Interview (selected participants)						X

Figure 3. Recruitment and Consent Flowchart: Rheumatology Clinic/ Occupational Therapy

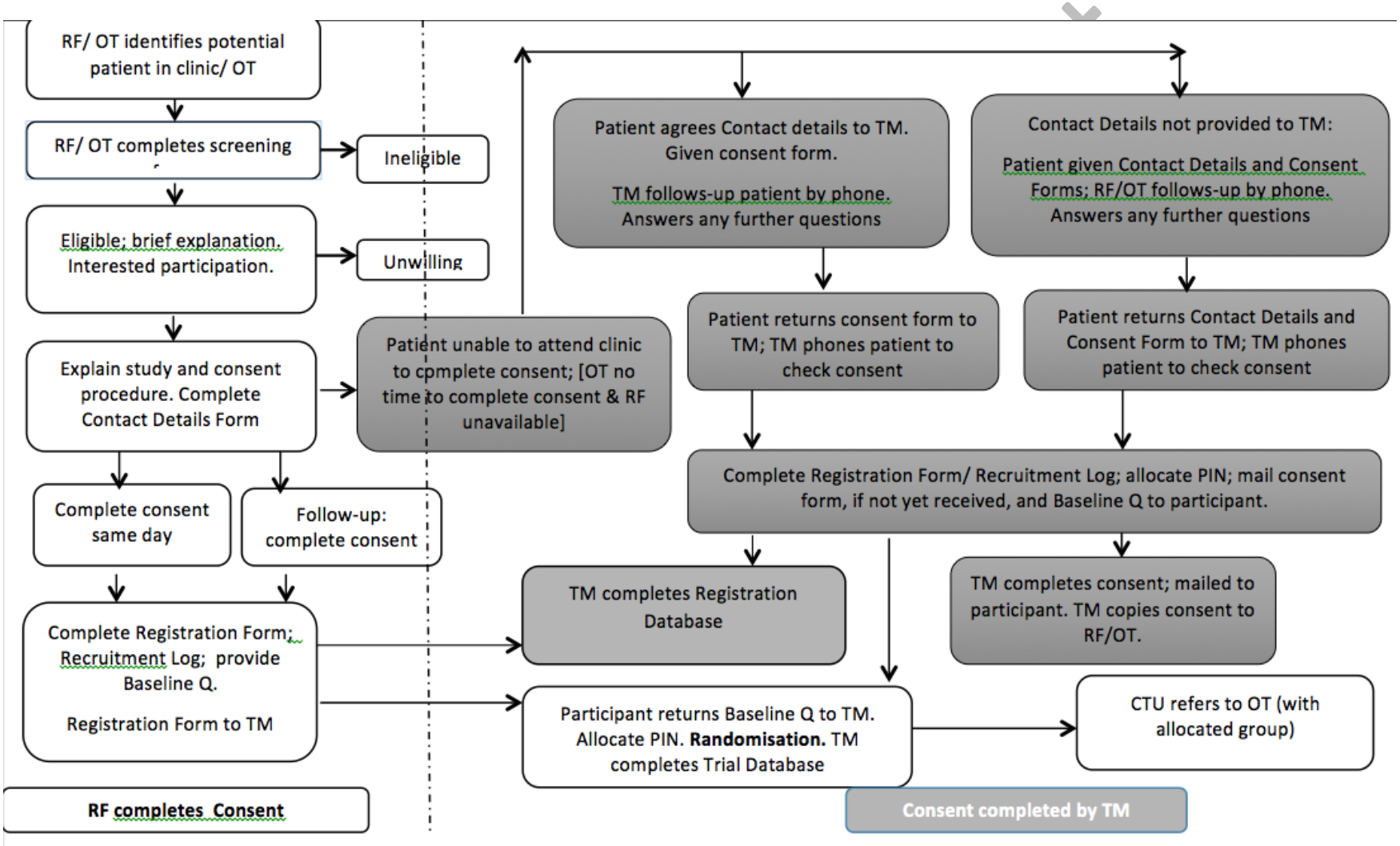
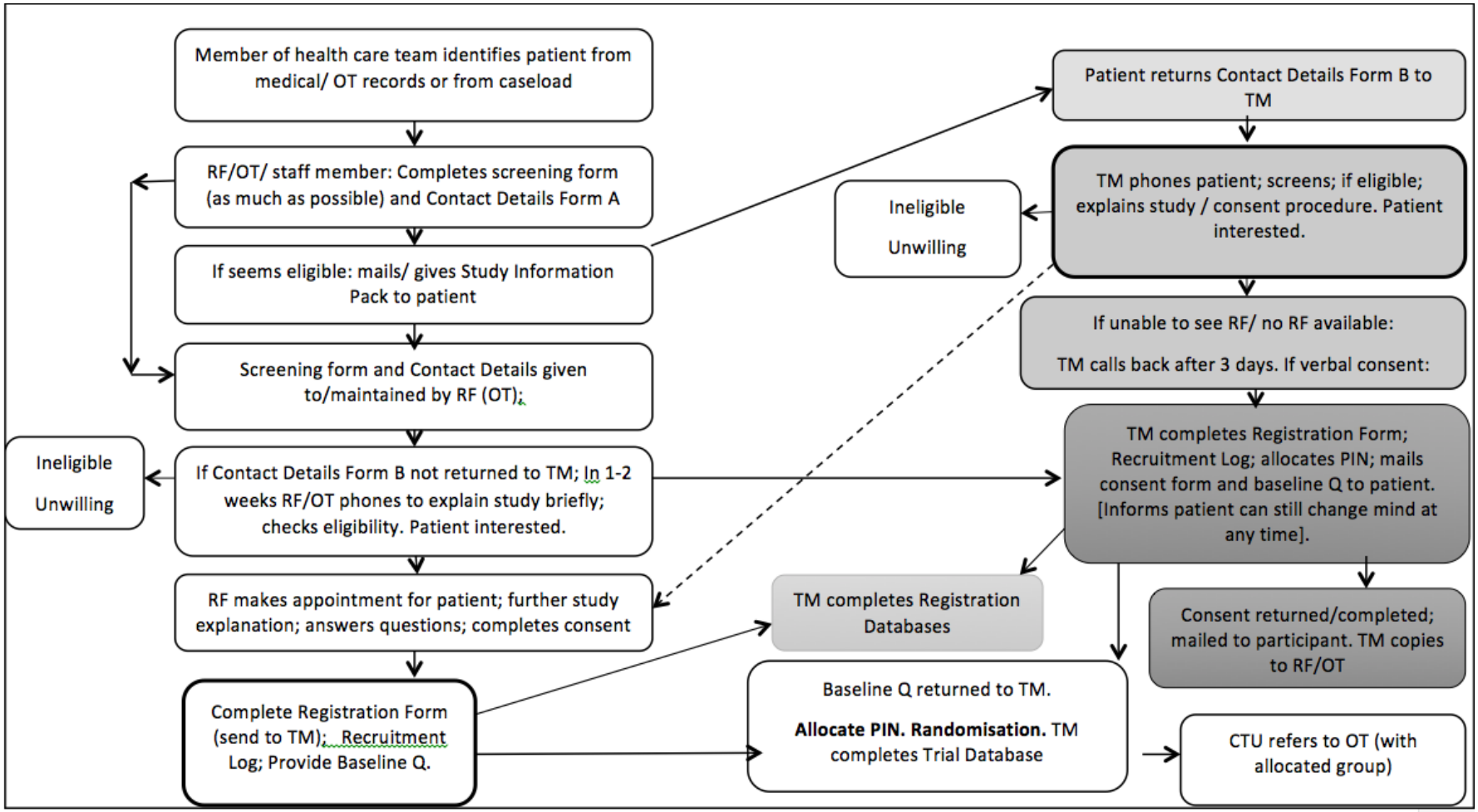


Figure 4. Recruitment Flowchart via Medical/OT Records / health care staff and Study Information pack mailed/provided to Patient


Member of health care team identifies patient from medical/ OT records or from caseload
RF/OT/ staff member: Completes screening form (as much as possible) and Contact Details Form A
If seems eligible: mails/ gives Study Information Pack to patient
Screening form and Contact Details given to/maintained by RF (OT);
If Contact Details Form B not returned to TM; In 1-2 weeks RF/OT phones to explain study briefly; checks eligibility. Patient interested.
RF makes appointment for patient; further study explanation; answers questions; completes consent
Complete Registration Form (send to TM); Recruitment Log; Provide Baseline Q.
Ineligible
Unwilling
Patient returns Contact Details Form B to TM
TM phones patient; screens; if eligible; explains study / consent procedure. Patient interested.
Ineligible
Unwilling
If unable to see RF/ no RF available:
TM calls back after 3 days. If verbal consent:
TM completes Registration Form; Recruitment Log; allocates PIN; mails consent form and baseline Q to patient. [Informs patient can still change mind at any time].
Consent returned/completed; mailed to participant. TM copies to RF/OT
TM completes Registration Databases
Baseline Q returned to TM.
Allocate PIN. Randomisation. TM completes Trial Database
CTU refers to OT (with allocated group)

[hospital/site headed paper]

PARTICIPANT INFORMATION SHEET:

A-GLOVES: Testing Arthritis Gloves in Rheumatoid/Inflammatory Arthritis

Part One: Introduction

We would like to invite you to take part in a research study. The study is being run by the Centre for Health Sciences Research, University of Salford. The Lancashire Clinical Trials Unit (CTU), (University of Central Lancashire) is also supporting the trial. Before you decide, you need to understand why the research is being done and what it will involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish. The research facilitator at your hospital will be happy to go through this information sheet with you. They can answer any questions you have. Alternately, our **Trial Manager, Dr Yeliz Prior** (0161 2950211 / 07471 826719 and y.prior@salford.ac.uk) can also do this on the telephone. Please ask if there is anything that is not clear to you or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of this study?

People with arthritis can have problems with hand pain, swelling and/ or stiffness. Occupational therapists may recommend they try wearing arthritis gloves. These might help relieve hand symptoms. Your Consultant Rheumatologist, Rheumatology nurse or occupational therapist helped identify this study might be relevant for you. We are testing two types of arthritis gloves to see if they are helpful or not for people with Rheumatoid or Inflammatory Arthritis.

We would like you to try wearing **one** pair of these gloves for up to 12 weeks. Which type of gloves you are given is randomly allocated by a computer. An occupational therapist fits these gloves for you.

You are asked to complete two questionnaires. One is completed at the beginning of the study, before you are given the gloves. The second is completed 12 weeks later, to find out if these arthritis gloves helped you or not.

The two types of arthritis glove we are testing look like this:

Both types of gloves leave the finger ends free. You can still use your hands as normal. The therapist discusses with you when it is best for you to wear these (during the day and/or night; how long for; for what activities). They are **not** worn all the time. You can leave them off at times when you need to. The gloves are washable.

There is no good quality research about whether these arthritis gloves work. Several small studies, done over 25 years ago, tested gloves worn at night by people with rheumatoid arthritis. Some studies found they helped and others did not. Since then, gloves have changed, treatment of arthritis has changed, gloves can be worn day and/or night; and a wider variety of people with arthritis are offered gloves. People with arthritis may find them helpful. We want to see whether these gloves have any effect. We are asking for your help with this study.

Why have I been invited?

We are asking people to take part who have:

1. **One** of two types of arthritis:

- Inflammatory arthritis (IA) or
- Rheumatoid arthritis (RA).

2. **Persistent** pain in your hand/s causing you one or more of the following:

- difficulty using your hand/s in the day
- disturbed sleep
- difficulty using your hand/s first thing in the morning

3. **Not** previously worn arthritis gloves and are willing to try wearing arthritis gloves in this study.

A member of your health care team identified this study may be relevant for you

Do I have to take part?

It is up to you to decide. Take your time to do so. Please discuss it further and ask questions with the person giving you this information. If you want to ask anything further, please call our **Trial Manager, Dr Yeliz Prior, on 0161 295 0211 or 07471 826719** (e-mail: y.prior@salford.ac.uk). Dr. Prior will be happy to answer any questions. (You can also send her the Contact Details Form in the FREEPOST envelope enclosed, if you are interested and want more information. Dr Prior can then call you).

If you decide not to take part, this will not affect the standard of care you receive. If you decide to take part, you can still withdraw at any time. You do not need to give a reason. This will not affect the standard of care you receive.

What will happen to me if I take part?

1. **If you decide to take part:** we will ask you to sign a consent form to show you agreed. The research nurse or occupational therapist at your hospital will complete the consent form with you.

If you cannot come to the hospital to complete the consent form, you can complete consent by telephone and mail with the A-GLOVES Trial Manager, Dr Yeliz Prior. Dr Prior would need your contact details to do this. The research nurse or occupational therapist, discussing the study with you, will **only** send your contact details to Dr Prior **if** you agree to this. Or please mail your contact details yourself to Dr Yeliz Prior on the Contact Details Form enclosed, using the FREEPOST envelope. Dr Prior will call you. She can then complete consent by telephone and mail with you.

2. Following consent, we will give/send you a questionnaire to complete at home. This questionnaire will ask about, for example, your age, gender, diagnosis and medication. It will also ask about your hand pain and stiffness, hand function and other health-related information. The questions are mostly answered using tick boxes/ circling numbers. It takes about 30 minutes to fill in. You do this in your own time at home. Then you post it back to us in the FREEPOST envelope provided (i.e. at no cost to yourself).

3. After you return the questionnaire, within 3 weeks you should receive an appointment with an occupational therapist. This will be at the Rheumatology /occupational therapy department you normally attend. The therapist will provide you with the arthritis gloves. We have trained the therapist to fit the gloves following our study instructions. You are asked to wear the same gloves you are fitted with for up to 12 weeks, as recommended. The therapist will discuss and agree with you when it is best for you to wear them. Sometimes, some people find gloves are itchy or hot if worn at night, or may have some tingling in the fingers. These feelings stop when you take the gloves off. The therapist will explain what to do should you have any minor problems. We ask you not to wear any other type of arthritis gloves during the 12 weeks of the study. After you have had the gloves for 2 to 4 weeks, the therapist will check the gloves with you. This will be at the hospital or may be by telephone. If you have any problems with or concerns about wearing the gloves before then or after, just contact the therapist.

4. At the end of the 12 weeks, we will send you a second questionnaire. This again asks about: your hand pain, stiffness, hand function and other health-related information. It also asks about: any changes in your medication and any other treatment you had in the last 12 weeks (such as physiotherapy). It asks how your hands are compared to before getting the gloves; whether you think the gloves help or not, and if you had any problems with them. This takes about 30 minutes. You do this in your own time at home. Then you post it back to us in the FREEPOST envelope provided.

5. Finally, we also want to interview **20-30 people**. You can let us know if you would like to be interviewed on the consent form. If you prefer not, it's not a problem. We don't need everyone to help. If you do agree to the interview, you can still change your mind at any time. In the interview, we ask your views about the gloves. For example: any benefits or negative effects of glove wear; and glove appearance and quality. The interview will be at a time and place that suits you. This can be in your own home or the hospital at which you were given your arthritis gloves. We would like to audio-record it to help us later in writing down accurately what you said. The recordings are only listened to by our research staff. Your name is not identified when these are typed up. These are only read by the researchers. We delete the recordings once the content is written down. We will not ask about any private information. Please do not disclose such information to the interviewer.

After you have completed the second questionnaire (and interview if you choose to do this), then we will send you a letter. This explains what to do about using the arthritis gloves in future. If you do not wish to keep them, simply throw them away in your household waste. They are not re-usable. If you want to try a different type of arthritis glove after you finish the study, please contact the OT.

Expenses and payments

There is no expense in completing the questionnaires, as we provide FREEPOST envelopes for the reply. We will pay back any travel costs you have attending clinics or occupational therapy to complete consent, to get the gloves and/ or for an interview. We provide a claim form. Please attach any receipts (for bus, train, parking) to this. Include the number of miles travelled if you come by car.

What are the possible benefits of taking part?

The study itself will not directly help you now, although you may find the gloves provided help you. The information you give us will help us understand any effects arthritis gloves may have on hand pain and function, and whether one type of arthritis glove is better than the other. In future, this will help therapists plan treatment for people with arthritis.

What are the possible disadvantages and risks of taking part?

The gloves are provided and fitted for your use by an occupational therapist at the hospital. The therapist has received training in fitting the gloves. We do not expect there are any disadvantages or risks to you in taking part in the study. If you choose to take part in the interviews, we will arrange these at a place and time to suit you.

If the information in Part 1 has interested you and you are considering taking part, please read the additional information in Part 2 before making any decision.

Part Two: Further information

Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice. We will handle all information about you in confidence. We will store it securely at the University of Salford and the Lancashire Clinical Trials Unit. All information which is collected about you during the course of the research will be kept strictly confidential. We only identify you in the interview recording by a number. You have the right to check the accuracy of the data held and correct any errors. Only staff involved in the research study see your information. Any direct quotes from the audiorecordings we use in reports, will not identify you in any way. We send a copy of your consent form to the hospital Consultant responsible for your care. This will be placed in your medical records.

What will happen if I don't want to carry on with the study?

You can withdraw from the study at any time, and your care will not be affected. However, we will use the data collected up until your withdrawal unless you tell us not to.

What will happen if there is a problem?

If you have problems with the arthritis gloves, please contact and discuss this with the occupational therapist who gave them to you. If you have queries about the study, questionnaires or interview, please contact our Trial Manager (Dr Yeliz Prior) who will answer these.

If you have any complaint about the way you have been dealt with during the study, or any possible harm you might suffer, we will address. If you have a concern about any aspect of this study, you should ask to speak first to: the occupational therapist who provided the arthritis gloves to you and the researchers. We will do our best to answer your questions (contact our Trial Manager: Dr Yeliz Prior on Tel: 0161 295 00211 or e-mail: y.prior@salford.ac.uk). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from:

The Customer Care Manager

Address of the participating hospital

Tel: xxxx

What will happen to the results of the research study?

We will send you a summary of the findings when the study is fully completed. When you finish taking part, we will send you a letter saying when this is likely to be.

We will write up the findings and submit them for publication. This will help Rheumatology and Occupational Therapy departments learn from our experiences. You will not be identified in any report or publication. We will send your occupational therapist a summary of the study when it is finished. We will also aim to present the study results at national and international rheumatology conferences. We will inform arthritis charities so they can choose whether to make the findings available to other people with arthritis via their websites/ magazines.

Who is organizing and funding the research?

The Centre for Health Sciences Research, University of Salford and the Lancashire Clinical Trials Unit are organizing this trial. We are working with the Occupational Therapy and Rheumatology departments at: Stepping Hill Hospital (Stockport), St Helens Hospital, Pennine Musculoskeletal Partnership Limited (Oldham), Trafford Hospital (Manchester), Leighton Hospital (Crewe), Victoria Infirmary (Northwich), Southport and Formby District General Hospital, Hexham General Hospital, North Devon District Hospital, Royal Hallamshire Hospital (Sheffield), Cannock Chase Hospital, New Victoria Hospital (Glasgow), Singleton Hospital (Swansea), Scunthorpe General Hospital, King's Mill Hospital (Sutton-in-Ashfield) and North Manchester General Hospital. We are also working with: Haywood Hospital (Stoke-on-Trent), Chapel Allerton Hospital (Leeds) and St Albans City Hospital/ Hemel Hempstead Hospital.

The study is funded by the **National Institute for Health Research (NIHR) through a Research for Patient Benefit (RfPB) grant.** The Chief Investigator is Professor Alison Hammond.

Who has reviewed the study?

All research in the NHS is looked at by independent groups of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favorable opinion by North of Scotland Research Ethics Committee 2. The Research Ethics Committee at the University of Salford and University of Central Lancashire have also approved the study.

Further information and contact details

If you have any questions about the study, wish to discuss taking part or have any concerns; please contact the researchers leading the study:

Dr Yeliz Prior – A-GLOVES Trial Manager

Centre for Health Sciences Research, University of Salford

L701 Allerton, Frederick Road, Salford M6 6PU

0161 295 0211 – 07471 826719

y.prior@salford.ac.uk

Professor Alison Hammond – Chief Investigator

Centre for Health Sciences Research, University of Salford

L701 Allerton, Frederick Road, Salford M6 6PU

Tel: 0161 295 0038 – a.hammond@salford.ac.uk

Information about the study is also available from our website: http://www.salford.ac.uk/rehabilitation-research/a-gloves-study

If you have any general queries about participating in research you can contact your hospital's Patient Advisory and Liaison Service (PALS). General information is also available on the Involve website (www.invo.org.uk). **INVOLVE** is a national advisory Group, funded by the Department of Health, which supports active public involvement in NHS, public health and social care research.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for

compensation against the NHS Trust at which you received the gloves and/or the University of Salford but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Finally

Thank you for considering taking part. Please keep this information sheet. We will ask you to sign a consent form if you agree to take part. We will give you a copy of this to keep.

[Hospital/site heading]

Site Number **Participant ID:**

A-GLOVES CONSENT FORM

Title of project: A-GLOVES: Testing Arthritis Gloves in Rheumatoid/Inflammatory Arthritis

Name of researcher: Prof Alison Hammond **Please INITIAL all boxes (i.e. do not tick)**

1. I confirm that I have read and understand the information sheet dated 8.7.15 (Version 1) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

3. If I do later choose to withdraw from the study, I agree that any data collected up to that point can be kept and used in the study. ☐

4. **Optional:** I agree to take part in the face-to-face interview about the gloves. I understand that the interview will be audio-recorded, recordings will be deleted once transcribed and anonymised quotes may be given verbatim in reports. ☐

5. I understand that relevant sections of my medical notes may be looked at by regulatory authorities or from the NHS Trust, where it is relevant for my taking part in this research. I give permission for these individuals to access my records. ☐

6. I agree to my Rheumatology Consultant, being informed of my participation in this study. ☐

7. I understand a copy of this form and my contact details will be forwarded to the research team at the University of Salford. ☐

8. I agree to take part in the above study. ☐

Name of patient:_____Date:_____**Signature:**_____

Name of person: taking consent:_____ Date:_____
Signature:_____

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	___1_____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	___4_____
	2b	All items from the World Health Organization Trial Registration Data Set	information in article_____
Protocol version	3	Date and version identifier	___2 & 24_____
Funding	4	Sources and types of financial, material, and other support	___2_____

Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	___1,2 & 24____
	5b	Name and contact information for the trial sponsor	___2_____
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	___24_____
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	___24 & 25____
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	_____5 - 7____
	6b	Explanation for choice of comparators	_____7_____
Objectives	7	Specific objectives or hypotheses	_____7_____

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	_____7_____
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	_____8+25____
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	_____8-9_____
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	_____9 & 10___
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	____10 +22__
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	____10 - 11
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	_____11

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12-14 & 30-33
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	____12 & 35-37
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	___14-15
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	____15 - 16

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	____16

Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	____ 16
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	_____16-17
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	_____ 17
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	_____18

Methods: Data collection, management, and analysis

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	____18 + 13-14
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	_____ 18-19

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	_____19
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	_____19-21
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	_____ 20-21
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	_____20_____

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	___ 25
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	____ 20-21
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	____ 21 & 22

Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	____ 22-23

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	_____ 2
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	_____25
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	____16
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	____N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	____ 19
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	____ 24

Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	____25_____
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	_____N/A
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	_____23_____
	31b	Authorship eligibility guidelines and any intended use of professional writers	____ 24
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	_____N/A____
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Additional file 1_
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.