The clinical and cost effectiveness of splints for thumb base osteoarthritis: a randomised controlled clinical trial

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Conflicts of interest

The authors have no conflicts of interest to declare

Abstract

Objectives: To investigate the clinical effectiveness, efficacy and cost effectiveness of splints (orthoses) in people with symptomatic basal thumb joint osteoarthritis (BTOA).

Methods: A pragmatic, multi-centre parallel group randomised controlled trial at 17 National Health Service (NHS) hospital departments recruited adults with symptomatic BTOA and at least moderate hand pain and dysfunction. We randomised participants (1:1:1) using a computer-based minimisation system to one of three treatment groups: a therapist supported self-management programme (SSM), a therapist supported self-management programme plus a verum thumb splint (SSM+S), or a therapist supported self-management programme plus a placebo thumb splint (SSM+PS). Participants were blinded to group allocation, received 90 minutes therapy over 8 weeks and were followed up for 12 weeks from baseline. AUSCAN hand pain at 8 weeks was the primary outcome, using intention to treat (ITT) analysis. We calculated costs of treatment.

Results: We randomised 349 participants to SSM (n=116), SSM+S (n= 116) or SSM+PS (n=117) and 292 (84%) provided AUSCAN hand pain scores at the primary end point (8 weeks). All groups improved, with no mean treatment difference between groups: SSM+S vs. SSM -0.5 (95% CI -1.4 to 0.4, p=0.255), SSM+PS vs. SSM -0.1 (95% CI -1.0 to 0.8, p = 0.829) and SSM+S vs. SSM+PS -0.4 (95% CI -1.4 to 0.5, p=0.378). The average 12-week costs were: SSM £586; SSM+S £738; and SSM+PS £685.

Conclusion: There was no additional benefit of adding a thumb splint to a high-quality evidence-based, supported self-management programme for thumb OA delivered by therapists.

Keywords: thumb splint, orthosis, symptomatic basal thumb joint osteoarthritis, clinical trial

Introduction

Background and objective

Osteoarthritis (OA) is a prevalent global condition with significant individual and socioeconomic impact [1]. Basal thumb OA (BTOA) affects the 1st carpometacarpal and/or scaphotrapezial joint and is a common form of hand OA that can cause pain, reduced functional performance, and impaired quality of life [2],[3]. Few effective options exist to treat and delay it's progression [4]. European League Against Rheumatism (EULAR) guidance recommends supported self-management approaches including education, exercises, assistive devices and splinting (orthoses) [5]. However, guidelines on splint provision are limited and there is no clear evidence for any advantage from including splinting within a package of supported self-management [6, 7]. No studies have examined the potential placebo/contextual effects of using splinting for BTOA [8]. A national research priority call to explore the most effective non-surgical interventions for treating painful hand arthritis [9] provided additional justification for this trial. We aimed to estimate the effectiveness, and cost-effectiveness of adding a verum or a placebo splint to an 8-week evidence-based, supported self-management package of out-patient care for people with symptomatic BTOA.

Methods

Design Overview

A pragmatic, multi-centre, parallel-group, participant-blinded, randomised controlled superiority trial (RCT) was conducted across 17 National Health Service (NHS) hospitals in England (Supplementary File 1) The trial was conducted between March 2017 and December 2018 by the Oxford Clinical Trials Research Unit (OCTRU), UK, approved by the Oxford C Research Ethics Committee, UK. (Ref:16/SC/0188) and monitored by Independent Trial Steering and Data Monitoring Committees (Supplementary File 2). The trial was registered (ISRCTN 54744256) and the protocol published [10].

Settings and Participants

Occupational therapists and physiotherapists (therapists) across 17 NHS sites who had attended trial training and completed Good Clinical Practice training [11] delivered the trial. Therapists identified consecutive potential participants from out-patient referrals and gave them an invitation letter, a participant information sheet and screened those interested in taking part. Adults aged >30 years with symptomatic BTOA reporting at least moderate hand pain (>5) and dysfunction (>9) on the Australian Canadian (AUSCAN) outcome measure [12], were screened using inclusion criteria (Supplementary File 3). All participants gave written informed consent to participate after which trial registration and baseline assessment were finalised.

Interventions

Participants were randomised to receive one of three treatments, each delivered over an 8 week period, specifically:

a) SSM: A supported self-management programme (Supplementary File 4) [10], based on clinical evidence [13], [14], [15], [16] national consensus [17] [18], and the trial's pilot study [19].

b) SSM+S: the SSM as above plus one of two verum thumb splints, either a Procool thumb CMC Restriction black splint or a beige Orfilight 2.5mm 3/32" micro perforated trouser leg splint custom made using a standard template (Figure 1).

c) SSM+PS: The SSM as above plus one placebo thumb splint with no apparent active biomechanical effect [20], [21], either a DMOrthotics thumb sleeve or a DMOrthotics thumb sleeve lite in black or beige (Figure1).

The splints chosen were informed following patient and clinician consultation [17], the pilot study [19] and grant funder feedback. Splints were prescribed using a splint decision protocol (Supplementary File 5) [10], a discussion with therapists around facilitators and barriers to splint wear, a splint wear diary and wear/care instructions (Supplementary File 4) [10].

Therapists conducted a 60-minute baseline appointment when participants agreed their self-management goals, signed an intervention contract, were given exercise and, when appropriate, splint wear adherence

diaries. At 2 weeks a telephone call was made to discuss progress and at week 4 a 30 minutes hospital appointment was scheduled to reinforce strategies to optimise adherence [22]. At week 8 participants re-visited the therapist to finalise trial procedures. We provided recommendations to carry out hand exercises "at least three times a week for at least 20 minutes each" and to wear splints for "a minimum of 6 hours a day".

There was no restriction to other concomitant general treatment during the trial. However, we requested that any intra-articular corticosteroid injection or surgical intervention was delayed until the end of the trial.

Randomisation, implementation and blinding

The OCTRU secure (encrypted) online randomisation service was used to record participant eligibility, stratification data and randomise participants into the study. Randomisation was on a 1:1:1 allocation ratio and stratified using; centre, baseline AUSCAN hand pain score [12] (scores of 6 to 12 vs. scores of 13 to 20) and treated hand dominance, to ensure parallel treatment groups were balanced for potential predictors of outcome. The first 30 participants were allocated to treatment arm using simple randomisation to seed the dynamic computer based minimisation algorithm which included a probabilistic element. Participants received treatment for one index thumb. If a participant had bilateral BTOA the most painful thumb was selected as the index. Participants were blinded to treatment allocation. Therapists had received training on how to deliver placebo splints convincingly [23] and were not blinded. Supplementary File 6 details strategies to maintain participant blinding.

Data collection

Self-report questionnaires were completed at baseline and 8 weeks during hospital appointments and at 12 weeks by post. Where 12 week questionnaires were not received within 3 weeks of issue a postal reminder was sent, if there was no response, minimal end-point data for AUSCAN hand pain were collected over the

phone. Up to 3 phone calls were made. The Grip Ability Test [24] was assessed at baseline, week 4 and 8 in the therapy department by a blinded assessor.

Outcomes

Self-report outcome measures were obtained at baseline, 8 and 12 weeks following randomisation. The primary outcome was the AUSCAN hand pain index [12] (ranges from 0 to 20 with higher values indicating worse outcomes) at 8 weeks. This was the most responsive standardised outcome measure from our pilot trial and permitted international data comparisons. Secondary outcomes included: the AUSCAN hand function index [12] (ranges from 0 to 36, with higher values indicating worse outcomes); the AUSCAN hand stiffness ordinal score [12] consisting of five ordinal categories (ranging from none to extreme hand stiffness); frequency of thumb pain over the past week using a 5 point ordinal visual analogue scale (VAS) (ranging from always to never) and intensity of thumb specific pain over the past week using a 5 point ordinal VAS (ranging from very mild to very severe). We assessed hand function performance without a splint using the Grip Ability Test (GAT) [24] where lower scores indicate better performance, at baseline, week 4 and week 8. We used the Michigan Hand Questionnaire [25] satisfaction with hand function question to record reported satisfaction with hand ability (ranges from 0 to 100, with higher scores indicating better outcomes). Work productivity over the last 7 days was recorded using the Work Productivity and Activity Impairment Questionnaire [26] (with ranges from 0 to 10 with higher values indicating worse outcomes). Leisure abilities were assessed using the leisure section of the Disability of the Arm, Shoulder, Hand questionnaire [27] that reported 5 levels of difficulty from no difficulty to unable to do, for recreational activities a) which require little effort, b) take some impact or force through the arm/shoulder or hand, and c) require the arm moves freely. We assessed self-efficacy using the Arthritis Self-Efficacy Pain Scale [28] (ranges from 1 to 10 with higher outcomes indicating better outcomes). Generic health related quality of life was reported using the SF12-V2 Physical Health Component Score (PCS) and Mental Health Component Scores (MCS) [29] (range 0–100; with high scores indicating high quality of life). We captured health status using the EuroQol 5

Dimensions 5-Levels (EQ-5D-5L) index questionnaire (range 0.59-1 where higher values indicate better health), and the EQ-5D-5L visual analogue scale (ranges from 0-100 with higher values indicating better outcomes) [30]. To calculate the OMERACT responder criteria [31] we used a Global Assessment of Change question and asked "With respect to your thumb base pain how would you describe yourself now as compared with the start of your trial treatment?" The response was provided on a 5 point Likert scale ranging from "very much worse" to "completely recovered". Responders were calculated in line with published guidelines [31] .

We provided quality assurance visits to NHS sites to maximise fidelity to trial intervention. Participants' self-reported adherence to exercise and daily splint wear was recorded using paper diaries. Adverse reactions and device deficiencies were recorded by therapists following standardised trial management procedures.

Sample Size

The sample size of 345 was calculated in the power and sample size package, PASS 11 (Hintze, J. (2011)). PASS 11. NCSS, LLC. Kaysville, Utah, USA. It was based on a global Analysis of Covariance (ANCOVA) of the primary endpoint across all three treatment arms, a target difference of 2 points with an assumed standard deviation of 5 (standardised effect size 0.4), based on pilot study data [19]. Using 80% power, a 5% significance level and allowing for up to 20% of loss to follow-up, 115 participants per arm (345 in total) were required. The sample size was not adjusted for multiple testing.

Statistical methods

The principal analysis of all outcomes was based on an a priori statistical analysis plan using intention to treat (ITT) and restricted to available data. The primary endpoint was also analysed using the per-protocol population (Supplementary File 8).

Continuous data were analysed using multilevel mixed-effects regression models including repeated measures of the relevant outcome at 8 and 12 weeks post randomisation (4 and 8 weeks post randomisation for grip

strength) (level 1) nested within participants (level 2). The model was adjusted for treated hand dominance, gender, age and the baseline value of the outcome variable. Time was added to the model as a categorical variable, and interactions between treatment and time were included. Clustering of outcomes by randomising centre was accounted for using the 'cluster' option in Stata's 'mixed' command and the use of robust standard errors.

Frequency and percentage of participants meeting binary endpoints were presented with unadjusted risk differences. Adjusted odds ratios were obtained from multilevel mixed-effects logistic models. Other categorical outcome variables were presented at each follow-up time point, with statistical comparisons between the treatment arms based on chi-squared tests. Sensitivity analysis for the primary endpoint at 8 weeks investigated the effect of participants with missing outcome data being, on average, up to 2 points worse or better than those with observed data.

For the economics evaluation, costs were estimated based on interventions received and follow-up healthcare resource use regardless of cause, applying unit costs from the Unit Costs of Health and Social Care compendium for 2017/2018 [32] and NHS National Schedule of Reference Costs 2017/2018. [33] Quality adjusted life years (QALYs) were derived from utilities; EQ-5D-5L responses were converted into utilities using the validated mapping function to derive utility values for the EQ-5D-5L from the EQ-5D-3L [34]. The incremental cost-effectiveness ratio (ICER) was calculated for all pairwise comparisons, using 1,000 bootstrap samples. We judged an intervention to be cost-effective if the ICER was £20,000 per QALY gained or below [35]. Full health economics evaluation methods are included in Supplementary File 9.

All analyses were performed in Stata 15.

Patient and public involvement and engagement

The trial was co-produced with NHS patients, expert clinicians and research partners with experience of living with BTOA [36],[17],[23],[19].

Results

Of 751 patients screened, 467 were eligible for inclusion and 349 participants were randomised; 116 to SSM, 116 to SSM+S, and 117 to SSM+PS (Figure 2). Baseline characteristics were well-balanced (Table 1). In the SSM group, 116 (100%) received SSM. In the SSM+S Group, 115 (99%) received SSM+S: 95 (82%) received a Procool Splint, and 20 (17%) received an Orfilight thermoplastic splint (for 1 (1%) the type of splint was not recorded). In the SSM+PS group, 114 (97%) received SSM+PS; 90 (77%) received a DMOrthotics Thumb Sleeve splint; 24 (21%) received a DMOrthotics Thumb Sleeve Lite; 2(2%) received a verum Procool Splint, and 1(1%) did not receive a splint. Two participants in the SSM group reported purchasing their own splint. Six participants in the SSM + PS group reported purchasing their own splint.

Table 2 provides estimates of treatment effect for the primary outcome at primary (8 week) and secondary (12 week) time points for both ITT and per-protocol populations. At 8 weeks, AUSCAN hand pain index scores were available for 95 (82%) in the SSM group; 96 (83%) in the SSM+S group, and 101(86%) of the SSM+PS group. At 8 weeks mean AUSCAN hand pain index scores had improved from baseline for all groups; 9.7 (SD 3.5) in the SSM group, 9.3 (SD 3.5) in the SSM+S group and 9.8 (SD 3.2) in the SSM+PS group. There was no evidence of a mean treatment difference in AUSCAN hand pain index scores at 8 weeks between groups, mean differences between groups being: SSM+S versus SSM -0.5 (95% CI -1.4, 0.4), p= 0.255; SSM+PS vs. SSM -0.1 (95% CI -1.0 to 0.8), p = 0.829; and SSM+S vs. SSM+PS -0.4 (95% CI -1.4 to 0.5), p=0.378. The treatment effects were neither statistically nor clinically significant in reducing hand pain between the 3 treatment arms at 8 weeks. Secondary time point analyses at 12 weeks did not change the overall clinical nor statistical significance. Analysis of the per-protocol population produced similar results and a 2-point difference sensitivity analysis for missing data (missing not at random assumption) (Supplementary File 10) also did not alter the results.

Fidelity

Self-reported daily adherence to hand exercises was similar between groups, all groups reporting decreasing

adherence over time. Reported splint wear adherence was similar between splint groups, placebo splint group participants tended to wear their splints longer each day than verum splint group participants. (Table 3).

Secondary outcomes

All secondary outcomes, (except the SF12-MCS and the EQ-5D-5L index at 8 weeks) showed no difference between treatment arms at primary and secondary end points. At 8 weeks the SF-12-MCS and the EQ-5D-5L index indicated a potential benefit of SSM vs. SSM+S and the SSM+PS respectively (Table 4). The global hypothesis test indicated no difference in outcomes between treatment arms at 8 and 12 weeks. Differences between treatment arms for the AUSCAN hand pain index pairwise comparisons were small, and fell below the target difference of two points, used in sample size calculations, to be considered clinically relevant.

Health Economic Results

Mean QALYS over the 12 week follow-up were estimated as 0.144 (95% CI 0.136 to 0.151) in the SSM group, 0.144 (95% CI 0.138 to 0.151) in the SSM+S group, and 0.144 (95% CI 0.136 to 0.151) in the SSM+PS group. The average overall cost over the 12 weeks intervention was £586 (95% CI: 389 to 865) for a participant receiving SSM, £738 (95% CI: 551 to 985) for a participant receiving SSM+S, and £685 (95 % CI: 506 to 895) for a participants receiving SSM+PS. Comparing interventions to SSM alone, the probability that SSM+S and SSM+PS were cost-effective was 28% and 32%, respectively. Supplementary File 11 details full health economics and cost effectiveness results.

Adverse Reactions

Ten adverse reactions were reported, affecting 3(3%) of SSM, 5(4%) of SSM+S and 2 (2%) of SSM+PS participants. None was serious and mostly related to hand pain lasting for longer than expected after performing the trial hand exercises. Eight device deficiencies, relating to wear and tear, were reported for 6 participants, 5(4%) in the SSM+S and 1(1%) in the SSM+PS group.

Blinding

Participant and GAT assessor blinding to treatment allocation was excellent. There was one potential participant un-blinding in the SSM+SP Group when the GP letter that detailed each treatment arm was sent to a participant in error. The trial team received no reported cases of GAT assessor unblinding through regular trial communication updates and quality assurance visits.

Withdrawals & Protocol deviations

Overall, 45 (13%) participants withdrew from the trial, 16 from the SSM group, 16 from the SSM+S group and 13 from the SSM+PS group. Reasons given included: the trial was too burdensome; too ill to continue; travel requirements; and withdrawal of consent. Protocol deviations were reported for 20 (6%) participants, 8 in the SSM, 6 in the SSM+S and 6 in the SSM+PS group. Seven (2%) of the protocol deviations were considered to be serious, specifically: 1 SSM participant and 1 SSM+S participant received thumb-base steroid injections; 1 SSM+S participant received thumb-base surgery; 2 participants in the SSM+PS group received verum splints in error and 2 received thumb-base steroid injections.

Discussion

In this multicentre RCT, we evaluated whether adding thumb-base splints (verum or placebo) to SSM delivered by occupational therapists and physiotherapists for patients with BTOA was more effective in reducing hand pain and disability than SSM alone. We found that adding thumb splints provided no additional clinical benefit to the 8 week SSM package. Pain and function improved from baseline to 8 and 12 weeks across all treatment groups, but there were no clinically relevant or statistically significant differences in outcomes between groups at either time-point. Adding splinting to SSM was not cost effective over 12 weeks compared with SSM alone. Thumb splints that used a biomechanical mode of action, aiming to support or immobilise the base of thumb, were not superior to thumb splints designed as biomechanical

placebo splints that permitted the thumb to move freely. This pragmatic trial recruited patients with painful, symptomatic base of thumb and our participants appear to represent hospital clinic populations with clinically significant symptomatic hand OA [37],[38],[39].

The strengths of this study include the extensive involvement of UK patient and clinical stakeholders in the trial development [17] ensuring our trial processes were practical and outcomes meaningful to stakeholders [18], [40]. This contributed to good recruitment rates, data quality and maintenance of participant blinding. To our knowledge we are the first team that has developed and designed two credible placebo thumb-base splints [36] with no known biomechanical components [20, 21]. We utilised health psychology approaches to optimise adherence to interventions but whilst self-reported adherence to exercises appeared high only half the participants reported wearing their splints as requested. . All groups at 4, 8 and 12 weeks reported carrying out the hand exercises, for the minimum time recommended, except those allocated to SSM+PS at 12 weeks. Self-reported splint wear indicated that almost half the participants reported wearing their splints for at least six hours a day for the first four weeks. Furthermore, by using pain as the primary outcome we were more likely to identify any contextual effects of splinting [41]. Finally, all participants received the same supported self-management from therapists, this was based on joint education approaches, that we have previously shown to improve pain self-efficacy [16], and cost-effective hand OA exercises [42].

Our trial is not without limitations. An 8 week intervention with a 12 week follow up may be too short to capture splint's potential impact, one trial has demonstrated that splints may improve outcome for up to 12 months [43] , However, in comparable BTOA splinting trials the average follow up was 8.1 weeks [44] with hand pain reduction occurring within 4-6 weeks , [45], [46] with hand pain stabilising for up to a year [47]. We aimed for a representative sample of outpatient therapy patients and did not exclude participants with concurrent hand conditions such as tendinitis, tenosynovitis de Quervain or carpal tunnel syndrome that could also cause thumb base pain. These possible co-morbid hand conditions may have contributed to our negative findings. We recruited predominantly white British participants attending secondary care NHS clinics and our findings may not be generalisable to community samples with milder BTOA or more ethnically diverse populations where features such as thumb hypermobility may be more prevalent [48]. We tested

our placebo splints for biomechanical impact but not their impact on proprioceptive feedback mechanisms [49].. There are no agreed classification criteria for BTOA. We classified BTOA using clinical symptomology and reported BTOA clinical symptoms within our sample [50], however, we did not collect data on interphalangeal or hand OA generally and we did not use international diagnostic criteria, nor radiographic evidence to confirm the presence and degree of hand OA . We used paper diaries for self-reported adherence to exercises and splint wear and we believe that more reliable methods are needed to capture adherence. Lastly, all groups received high quality evidence-based SSM and all improved during the trial, the benefits from SSM may be sufficiently large to outweigh any smaller additional benefits that splints may have contributed.

Clear guidelines on splint provision are limited, and recent systematic reviews conclude that there are no clear indications for splinting in addition to a package of supported self-management for BTOA [6, 7]. Our study presents contemporary evidence for the clinical and cost-effective management of BTOA and the potential role of splinting.

In summary, our results demonstrate that all groups receiving high quality evidence-based, supported self-management improved hand pain, function and quality of life outcomes. Our evidence shows no difference in short-term patient-centred outcomes between verum and placebo splints, and no apparent benefit from adding either splint to a therapist-supported self-management programme**.**

Rheumatology key messages:

1. Thumb splinting provided no additional benefit for hand pain in both hands over supported self-management
2. Thumb splinting provided no additional benefit over a biomechanical placebo thumb splint
3. Different mechanisms of action for thumb splints may exist that are not captured through pain and function measures.

References

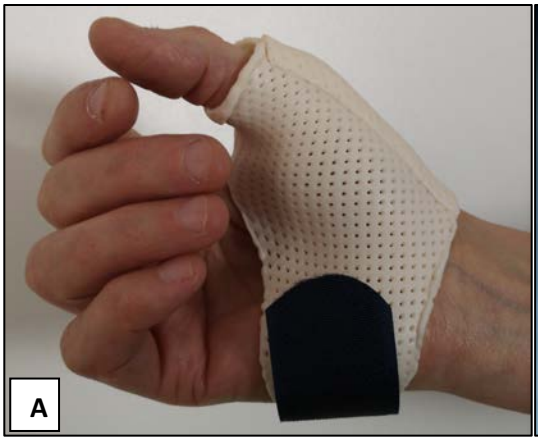
1. Murray, C.J.L., et al., *Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition.* The Lancet, 2015. **386**(10009): p. 2145-2191.
2. Marshall, M., et al., *Subsets of symptomatic hand osteoarthritis in community-dwelling older adults in the United Kingdom: prevalence, inter-relationships, risk factor profiles and clinical characteristics at baseline and 3-years* Osteoarthritis and Cartilage2013. **21**(11): p. 1674-1684.
3. Van Den Ende, C., et al., *Thumb base involvement in established hand osteoarthritis* Annals of the Rheumatic Diseases, 2013. **72**(S3): p. 784.
4. Kroon, F.P.B., et al., *Efficacy and safety of non-pharmacological, pharmacological and surgical treatment for hand osteoarthritis: a systematic literature review informing the 2018 update of the EULAR recommendations for the management of hand osteoarthritis.* RMD Open, 2018. **4**(2): p. e000734.
5. Kloppenburg, M., et al., *2018 update of the EULAR recommendations for the management of hand osteoarthritis.* Ann Rheum Dis, 2019. **78**(1): p. 16-24.
6. Buhler, M., et al., *Effectiveness of splinting for pain and function in people with thumb carpometacarpal osteoarthritis: a systematic review with meta-analysis.* Osteoarthritis and Cartilage, 2019. **27**(4): p. 547-559.
7. Kjeken, I., et al., *Effect of assistive technology in hand osteoarthritis: a randomised controlled trial.* Annals of the Rheumatic Diseases, 2011. **70**(8): p. 1447-1452.
8. Zou, K., et al., *Examination of overall treatment effect and the proportion attributable to contextual effect in osteoarthritis: meta-analysis of randomised controlled trials.* Annals of the Rheumatic Diseases, 2016. **75**(11): p. 1964-1970.
9. James Lind Alliance. *Common Conditions Affecting the Hand and Wrist Top 10*. 2017 [cited 2019 01/01/2019]; Available from: http://www.jla.nihr.ac.uk/priority-setting-partnerships/common-conditons-affecting-the-hand-and-wrist/top-10-priorities.htm.%202017;.
10. Adams, J., et al., *The Osteoarthritis Thumb Therapy (OTTER) II Trial: a study protocol for a three-arm multi-centre randomised placebo controlled trial of the clinical effectiveness and efficacy and cost-effectiveness of splints for symptomatic thumb base osteoarthritis.* BMJ Open, 2019. **9**(10): p. e028342.
11. NIHR. *Good Clinical Practice* 2019 [cited 2019 01/03/2019]; Available from: https://www.nihr.ac.uk/our-research-community/clinical-research-staff/learning-and-development/national-directory/good-clinical-practice/.
12. Bellamy, N., et al., *Clinimetric properties of the AUSCAN Osteoarthritis Hand Index: an evaluation of reliability, validity and responsiveness.* Osteoarthritis Cartilage, 2002. **10**(11): p. 863-9.
13. Kjeken, I., et al., *Systematic Review of Design and Effects of Splints and Exercise Programs in Hand Osteoarthritis.* Arthritis Care & Research, 2011. **63**(6): p. 834-848.
14. Dziedzic, K., et al., *Self-management approaches for osteoarthritis in the hand: a 2x2 factorial randomised trial.* Ann Rheum Dis, 2015. **74**(1): p. 108-18.
15. Lamb, S.E., et al., *Exercises to improve function of the rheumatoid hand (SARAH): a randomised controlled trial.* Lancet, 2015. **385**(9966): p. 421-9.
16. Dziedzic, K.S., et al. *Self management, joint protection and exercises in hand osteoarthritis: a randomised controlled trial with cost effectiveness analyses*. BMC musculoskeletal disorders, 2011. **12**, 156 DOI: 10.1186/1471-2474-12-156.
17. Barbosa Boucas, S., et al., *Defining optimal NHS occupational therapy treatment, individualized splint and placebo splint for patients with thumb base OA: a Delphi study.* Rheumatology 2013a. **52**(S1): p. i105.

18. Hislop, K., et al., *Patient and public involvement (PPI) in informing the osteoarthritis of the thumb therapy (OTTER) pilot trial: What matters most to people with thumb base osteoarthritis. .* Annals of the Rheumatic Diseases, 2013. **72**(S3): p. 778.
19. Adams, J., et al., *The Effectiveness and Efficacy of Splints for Thumb Base Osteoarthritis: A Pilot Randomized Controlled Trial.* Rheumatology, 2014. **53**(suppl_1): p. i41-i42.
20. Loyley, M.S.T., et al., *Comparison of the functional impact of verum and placebo thumb base orthoses: a proof of concept study.* Rheumatology, 2019. **58**(Supplement_3).
21. Davis, L., et al., *Comparison of impact of verum and placebo thumb base orthoses on skin surface temperature and pressure: a proof of concept study* Annals of the Rheumatic Diseases, 2019. **78**(Suppl 2): p. 1052-1052.
22. Michie, S., et al., *Behaviour change techniques: the development and evaluation of a taxonomic method for reporting and describing behaviour change interventions (a suite of five studies involving consensus methods, randomised controlled trials and analysis of qualitative data).* Health Technol Assess, 2015. **19**(99): p. 1-188.
23. Jones, L., et al., *The Thoughts and Feelings Held by Clinicians about the delivery of a Placebo Thumb Splint in an Osteoarthritis Rehabilitation Trial.* Hand Therapy, 2013. **18**(3): p. 77-83.
24. Dellhag, B. and A. Bjelle, *A grip ability test for use in rheumatology practice.* The Journal of Rheumatology, 1995. **22**(8): p. 1559-1565.
25. Chung, K.C., et al., *Reliability and validity testing of the Michigan Hand Outcomes Questionnaire* The Journal of Hand Surgery 1998. **23A**(4): p. 575-587.
26. Reilly, M.C., A.S. Zbrozek, and E.M. Dukes, *The validity and reproducibility of a work productivity and activity impairment instrument.* Pharmacoeconomics, 1993. **4**(5): p. 353-65.
27. Hudak, P.L., P.C. Amadio, and C. Bombardier, *Development of an upper extremity outcome measure: The DASH (Disabilities of the Arm, Shoulder and Hand).* American Journal of Industrial Medicine 1996. **29**: p. 602-608.
28. Lorig, K., et al., *Development and evaluation of a scale to measure self-efficacy in people with arthritis.* Arthritis Rheum, 1989. **32**(1): p. 37-44.
29. Ware, J., M. Kosinski, and S. Keller, *A 12-Item Short-Form Health Survey: Construction of scales and preliminary tests of reliability and validity.* Med Care, 1996. **34**: p. 220-223
30. Euroqol Group, *Euroqol: a new facility for the measurement of health-related quality of life.* Health Policy, 1990. **16**: p. 199-208.
31. Pham, T., et al., *OMERACT-OARSI initiative: Osteoarthritis Research Society International set of responder criteria for osteoarthritis clinical trials revisited.* Osteoarthritis Cartilage, 2004. **12**(5): p. 389-99.
32. Personal Social Services Research. *Unit Costs of Health and Social Care 2018*. 2019 [cited 2019 23/05/2019]; Available from: https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2018/.
33. NHS Improvement. *Reference Cost Collection: National Schedule of Reference Costs - Year 2017-18*. 2018 [cited 2019 23/05/2019]; Available from: https://improvement.nhs.uk/resources/reference-costs/#rc1718
34. van Hout, B., et al., *Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets.* Value Health, 2012. **15**(5): p. 708-15.
35. Excellence., N.I.f.H.a.C. *Guide to the methods of technology appraisal 2013*. 2013 [cited 2018 21/11/2018]; Available from: https://www.nice.org.uk/process/pmg9/chapter/foreword.
36. Gooberman Hill, R., et al., *Designing a placebo device: involving service users in clinical trial design.* Health Expectations 2013. **16**(4): p. e100–e110.
37. Wolf, J.M., et al., *Occupational load as a risk factor for clinically relevant base of thumb osteoarthritis.* Occupational and Environmental Medicine, 2020. **77**(3): p. 168-171.
38. Wouters, R.M., et al., *Exercise Therapy in Addition to an Orthosis Reduces Pain More Than an Orthosis Alone in Patients With Thumb Base Osteoarthritis: A Propensity Score Matching Study.* Arch Phys Med Rehabil, 2019. **100**(6): p. 1050-1060.

39. Haugen, I.K., et al., *Prevalence, incidence and progression of hand osteoarthritis in the general population: the Framingham Osteoarthritis Study.* Annals of the rheumatic diseases, 2011. **70**(9): p. 1581-1586.
40. Barbosa Boucas, S., et al., *Differences between service providers and users when defining feasible optimal NHS occupational therapy treatment for patients with thumb base OA: Results from a Delphi study.* Annals of the Rheumatic Diseases 2013b. **72**(S3): p. 779-780.
41. Huang, Z., et al., *Meta-analysis of pain and function placebo responses in pharmacological osteoarthritis trials.* Arthritis Res Ther, 2019. **21**(1): p. 173.
42. Oppong, R., et al., *Joint protection and hand exercises for hand osteoarthritis: an economic evaluation comparing methods for the analysis of factorial trials.* Rheumatology (Oxford), 2015. **54**(5): p. 876-83.
43. Rannou F, Dimet J, Boutron I, et al. Splint for base-of-thumb osteoarthritis: a randomized trial. *Ann Intern Med*. 2009;150(10):661-669.
44. Baradaran, A., et al., *Comparison of Custom-made Versus Prefabricated Thumb Splinting for Carpometacarpal Arthrosis: A Systematic Review and Meta-analysis.* Arch Bone Jt Surg, 2018. **6**(6): p. 478-485.
45. Valdes, K., N. Naughton, and M.A. Szelwach, *Patient satisfaction with the CMC controller: A cohort study.* J Hand Ther, 2020.
46. Arazpour, M., et al., *The effect of thumb splinting on thenar muscles atrophy, pain, and function in subjects with thumb carpometacarpal joint osteoarthritis.* Prosthet Orthot Int, 2017. **41**(4): p. 379-386.
47. Tsehaie, J., et al., *Predicting Outcome After Hand Orthosis and Hand Therapy for Thumb Carpometacarpal Osteoarthritis: A Prospective Study.* Arch Phys Med Rehabil, 2019. **100**(5): p. 844-850.
48. Vaughn, I.A., et al., *Racial-Ethnic Differences in Osteoarthritis Pain and Disability: A Meta-Analysis.* J Pain, 2019. **20**(6): p. 629-644.
49. Marks, R., *Osteoarthritis and Proprioception: What Does the Literature Reveal?* International Journal of Orthopaedics, 2017. **4**(5): p. 826-836.
50. Mbanasor, E., et al., *An exploration of the clinical and functional characteristics of a thumb base osteoarthritis cohort.* Rheumatology, 2020. **59**.

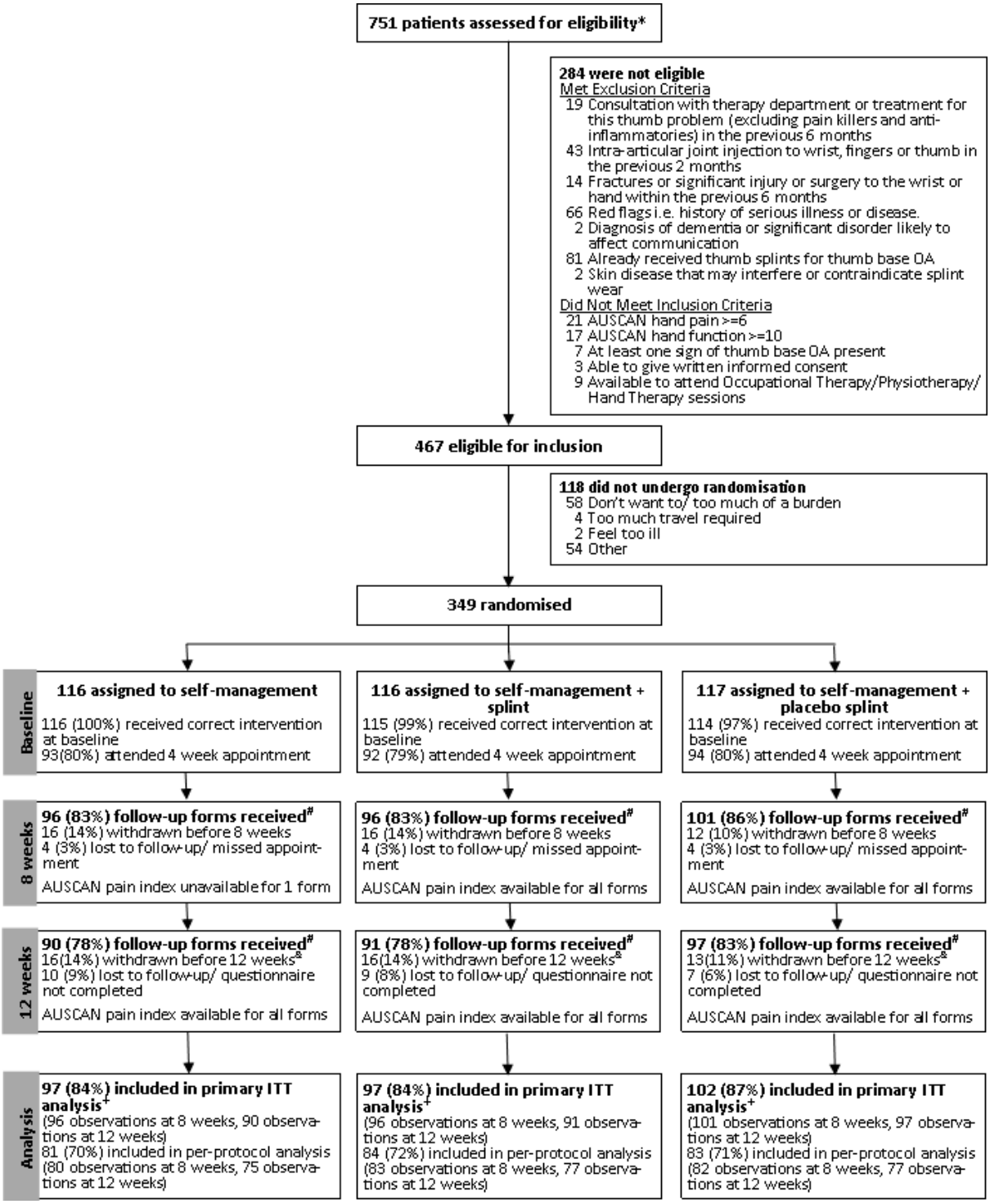
*** PLEASE NOTE THAT FURTHER TO EDITORIAL TEAM REQUESTS ADDITIONAL PHOTOGRAPHS HAVE BEEN EMAILE DSEPARATELY AS ARE TOO LARGE TO EMBED WITHIN THIS DOCUMENT. THE EDITORIAL TEAM HAS REQUESTED LARGER FILES SO THAT THE FIGURES ARE NOT PIXELATED ON PUBLICATION – THEREFORE THESE IMAGES WILL BE UPGRADED FOR THE PUBLICATION IN LINE WITH WHAT HAS ALREADY BEEN EMAILED TO THE TEAM. **Figure 1 Trial Splints**

A = Orfilight thermoplastic splint **B= Promedics Procool thumb restriction splint**



C= DMOrthotics thumb sleeve **D= DMOrthotics thumb sleeve lite**

Figure 2: Trial CONSORT diagram



Complete screening data was available from all 17 sites; #This includes both patient questionnaires, and AUSCAN

hand pain index data received by phone follow-up; [&]This includes all withdrawals up to 12 weeks (and also includes those reported at the 8 week follow-up);
[+]The primary analysis model is a multilevel mixed-effects model and utilises data from all participants with at least one follow-up observation.

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Role of the Funding Source

Versus Arthritis (Formerly Arthritis Research UK) approved the appointment of a Trial Steering Committee and Data Management Committee to scrutinise and oversee the running of this trial. The funder had no part in data analysis, interpretation nor dissemination.

DMOrthotics and Promedics did not fund any part of this work. They had no part in the design, conduct, analysis nor reporting of the trial and remained independent throughout. All splints used for the trial were purchased.

Trial Registration

The trial registration is ISRCTN 54744256

Data Availability Statement

The data underlying this article are available in the article and in its online supplementary material.

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