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Original article

Effect of preformed foot orthoses in reducing pain in children with juvenile idiopathic arthritis: a multicentre randomized clinical trial

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Abstract

Objectives. The aim of this study is to investigate the effect of customized preformed foot orthoses on pain, quality of life, swollen and tender lower joints and foot and ankle disability in children with JIA.

Methods. Parallel group design. Children diagnosed with JIA were recruited from the three children's hospitals in New South Wales, Australia. Participants were randomly assigned to a control group receiving a standard flat innersole (sham) with no corrective modifications. The trial group were prescribed a preformed device that was customized based on biomechanical assessments. Pain was the primary outcome and was followed up to 12 months post intervention. Secondary outcomes include quality of life, foot and ankle disability and swollen and tender joints. A linear mixed model was used to assess the impact of the intervention at each time point.

Results. Sixty-six participants were recruited. Child-reported pain was reduced statistically and clinically significant at 4 weeks and 3 months post intervention in favour of the trial group. Statistical significance was not reached at 6 and 12-month follow-ups. Quality of life and foot and ankle disability were not statistically significant at any follow-up; however, tender midfoot and ankle joints were significantly reduced 6 months post intervention.

Conclusion. Results of this clinical trial indicate customized preformed foot orthoses can be effective in reducing pain and tender joints in children with JIA exhibiting foot and ankle symptoms. Long-term efficacy of foot orthoses remains unclear. Overall, the trial intervention was safe, inexpensive and well tolerated by paediatric patients.

Trial registration. Australian New Zealand Clinical Trials Registry (ANZCTR): 12616001082493.

Key words: foot orthoses, JIA, juvenile idiopathic arthritis, lower limb, paediatrics

CLINICAL SCIENCE

Rheumatology key messages

- Foot orthoses (FOs) significantly reduce lower limb joint tenderness and pain in children with JIA.
- The long-term effect of customised preformed FOs remains unclear.
- Future clinical trials may explore the effect of custom versus customised FOs in children with JIA.

Introduction

JIA is the most common rheumatic disease in children and adolescents [1]. It has an incidence of 1–2 in every 1000 before the age of 16 [2]. The lower extremity is commonly involved in JIA, with the knee and ankle prevalent in at least 50% of patients at disease onset [3]. Joints of the feet such as the sub-talar, talo-navicular and calcaneo-cuboid appear to be the most common sites of foot disease in JIA [4]. Synovitis is the underlying clinical manifestation in JIA, leading to joint swelling, pain, stiffness and secondary physical problems [1]. The implications of delayed diagnosis and treating foot and ankle problems in JIA can be severe. One recent survey

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in New South Wales (NSW, Australia) reported 42.6% ($n = 63$) of participants with a rheumatic disease experienced delays in diagnosis for up to 6 months [5]. Clinicians specializing in the lower limb such as podiatrists can assist the multidisciplinary paediatric rheumatology team with early gait analysis and biomechanical evaluation and prompt targeted lower limb physical [6] and mechanical therapies [7].

Foot orthoses (FOs) are typically prescribed by podiatrists to reduce pain, disability and improve function and quality of life in a range of different diseases and mechanical problems [8–12]. Three clinical trials have previously explored the effect of podiatric interventions in JIA [13–15]. Two randomized clinical trials evaluated the effect of FOs alone [13, 14] and the third trial combined intra-articular corticosteroid injections with FOs [15]. A recent systematic review with meta-analysis combining both FOs clinical trials showed broad CIs with insignificant differences between custom or customized FOs *vs* a control device in outcomes including pain and quality of life [7]. Hendry *et al.* (2013) explored the effect of a multidisciplinary foot care program including the use of intra-articular corticosteroid injections and customized FOs [15]. The primary outcome was foot and ankle disability with authors reporting no significant differences between trial and control groups over a 12-month data collection. Overall, there is inconclusive evidence to support the use of FOs in children with JIA. No clinical trials have explored the effect of FOs alone on pain beyond 6 months and lower limb joint swelling and tenderness in JIA.

The aim of this clinical trial is to explore within a 12-month period the effect of customized FOs in reducing pain, foot and ankle disability, swollen and tender joints, and improving quality of life in children and adolescents with JIA.

Methods

A prospective, parallel group, multicentre single-blinded RCT was conducted in NSW, Australia from 2018 to 2020. Recruitment and data collection were conducted at the Sydney Children's Hospitals Network (Westmead and Randwick), and the John Hunter Children's Hospital (Newcastle).

The protocol is published and available as open access (http://dx.doi.org/10.1136/bmjpo-2017-000121).

Ethics were approved by the Hunter New England Human Research Ethics Committee (16/09/21/4.03). Site authorization was then approved for the Sydney Children's Hospital Network (SSA/16/SCHN/436) and John Hunter Children's Hospital (SSA/16/HNE/472) research governance committees.

Participants

Table 1 displays the eligibility criteria for participants. Paediatric rheumatologists D.S.-G. and J.C. independently identified potentially eligible participants from their respective hospital outpatient clinics. Potentially eligible participants were referred to chief investigator A.F. who provided the study information sheets. All parents or guardians of participants provided written informed consent then were randomly assigned to receive either a control or trial intervention. Team researcher (A.C.) who was independent of recruitment and data collection generated the randomization sequence in blocks of 10 (http://www.randomization.com). Allocation concealment was achieved by A.C. masking the sequence into consecutively numbered sealed and opaque envelopes. Sealed envelopes were strictly opened by the chief investigator (A.F.) only on the day of the participant's baseline consultation to reveal the allocated intervention group.

Intervention

The control group received a sham device made from a flat 1 mm leather board and with no corrective modifications. The trial group received customized preformed FOs. The preformed device (SlimFlex Simple, Algeos PTY LTD) was full-length and made from low-density EVA. The customization options adopted in the trial group are displayed in Supplementary Table S1, available at *Rheumatology* online. The top cover for both

Table 1 Inclusion and exclusion criteria for enrolling participants

Inclusion	Exclusion
• Diagnosis of JIA according to the International League of Associations for Rheumatology (ILAR) criteria • Aged 5–18 years • Active involvement of the lower limb (must include at least foot/and or ankle) • No previous use of FOs or previous failure of foot orthotic management where the patient has not worn any FOs for a period of at least 3 months • If disease-modifying antirheumatic drugs and/or biological therapy are used, not having started these drug therapies within 6 months of enrolling in the trial	• Currently using FOs • Inability to walk barefoot or shod for 15 m without assistive devices • Concomitant musculoskeletal disease • Central or peripheral nerve disease and endocrine disorders, including diabetes mellitus • History of lower limb surgery that required general anaesthetic • Where prescription of FOs is contraindicated, for example • Unwillingness to wear appropriate footwear for fitting orthoses

intervention groups was 1.5 mm with neoprene base and a stretchable hypoallergenic nylon top. This approach was used to increase blinding of participants to their intervention and to observe dynamic impressions on the FOs, suggesting compliance of use. A.F. conducted all the biomechanical assessments and prescription of all FOs across each recruitment site. Validated biomechanical measurements, such as the foot posture index and physical examination of joints, were obtained at baseline prior to prescription of the trial and control FOs.

Following the biomechanical assessment, devices were fitted on the same day of the initial consultation (baseline). Participants in both groups received standard footwear advice and continued their standard clinical care. Adherence to intervention has been emphasized by supplying a specific 'FOs diary'. Participants in both groups were asked to record their compliance in wearing the FOs every week for the duration of the trial. Changes in medication were also recorded over the 12-month period. This was to reduce confounding in the hope that any perceived differences were due to FOs prescription and not changes in medication.

Outcome measures

Pain

Pain was the primary outcome and measured using a visual analogue scale (VAS). This has been validated in children with JIA, with a minimally important clinical difference between intervals of 8 mm [16]. In accordance with the two previous clinical trials for FOs alone in JIA [13, 14], self-reported pain was chosen as the primary outcome. Pain was measured at baseline, 4-week, 3, 6 and 12-months post intervention prescription. Participants were asked to rate their lower limb pain on a 100 mm VAS. A low score indicates less pain and therefore a better outcome. Parents were also asked to rate their child's pain using the same scale based on their current perception.

Quality of life

Quality of life was assessed as a secondary outcome in this trial and was measured using the Pediatric Quality of Life (PedsQL), Rheumatology Module (version 3.0) [17]. Quality of life was measured at baseline, 3, 6 and 12 months post intervention prescription. Similarly to pain, this outcome is self-reported, with both child and parents required to complete the questionnaires. The questionnaires are available in different age ranges including ages 5–7, 8–12 and teen (13+).

Foot and ankle disability

The juvenile arthritis foot ankle disability index (JAFI) was used to measure foot and ankle disability. The JAFI is 27-item self-reported, validated, questionnaire specific to the foot and ankle of children and adolescents with JIA [18]. The JAFI is divided into three main components: physical impairment; activity limitation; and participation restriction. Foot and ankle disability were measured at baseline, 3, 6 and 12 months post intervention prescription.

Swollen and tender joints

Swollen and tender joints were measured by two experienced paediatric rheumatologists. Both were blinded to the participants intervention during the trial. Swollen and tender joints were recorded using a modified foot and ankle PE tool, originally designed for adults with RA [19]. As part of this JIA trial, the original tool was modified to include 20 joints per side, specifically: hip; knee; ankle; sub-talar; calcaneo-cuboid; talo-navicular; metatarsophalangeal; proximal interphalangeal; and distal interphalangeal. This outcome was measured at baseline and at 6 months.

Sample size

Power calculations were based on the primary outcome of pain measured on a 100 mm VAS, with a minimal clinical significance of 8 mm. For a two-sided *t* test with $\alpha = 0.05$ and power 80% for a randomized controlled trial design with baseline and primary outcome of difference between the groups at 12 months, and a moderate effect size of 0.6, it was estimated that a total of 90 participants would be required (45 controls and 45 trial) on a ratio of 1:1 allocation. This was adjusted with an analysis of covariance using an assumed correlation of 0.6 giving an adjusted total number of participants required of 60 (30 controls and 30 trial). The study was be overpowered to an estimated 66 (i.e. 33 participants per group) to allow for 10% dropouts during the 12-month data collection period.

Statistical analysis

All statistical analyses were conducted using Stata v14.0 (StataCorp Ltd, College Station, TX, USA). Statistical support was acquired after the protocol was published and therefore changes in statistical analysis methods can be seen between the protocol and final RCT manuscripts. Participant characteristics at baseline were compared descriptively by treatment group with means, S.D. or frequencies and percentages where appropriate.

All outcomes were summarized with means and S.D. at each time point. A linear mixed model was used to assess the impact of the intervention at each time point. A random intercept effect for individuals was included to account for repeated measures. Time as categorical with a time by group allocation interaction and the outcome at baseline were also included. Estimates with 95% CIs and *P*-values are presented.

The outcomes, joint swelling and tenderness were summarized with means and SD., median and range (min, max) at baseline and 6 months. Negative binomial regression with a log link function was used to assess the difference between treatment groups at 6 months. Joint groups that were deemed to have insufficient data were not analysed and modelled to avoid overfitting.

Rate ratios with 95% CIs and *P*-values are provided. *P*-values <0.05 were considered statistically significant.

Results

Figure 1 depicts the participant timeline. Table 2 includes participant characteristics by intervention group. Participant demographics including age and sex were similar between groups, as was the mean years of disease duration. The most commonly prescribed drug therapy in both groups was MTX followed by a combination of MTX and a biologic drug. Control group participants were taking more NSAIDs, prednisone and combination therapies of NSAIDs, MTX and biologics. This may suggest the control group participants had slightly worse disease than the trial group.

Primary outcome

After 4 weeks post intervention, the trial group (mean = 26.81 mm, S.D. = 23.11) averaged a reduction in pain of 14.92 mm on a 100 mm VAS compared with the control group (mean = 40.97, S.D. = 28.82). This was both statistically and clinically significant with *P*-value of 0.018 and 95% CIs of −27.30 mm to −2.55 mm. The 3-month post intervention resulted in a large average reduction of pain in the trial group (mean = 16.87 mm, S.D. = 14.78)

FIG. 1 Participant timeline

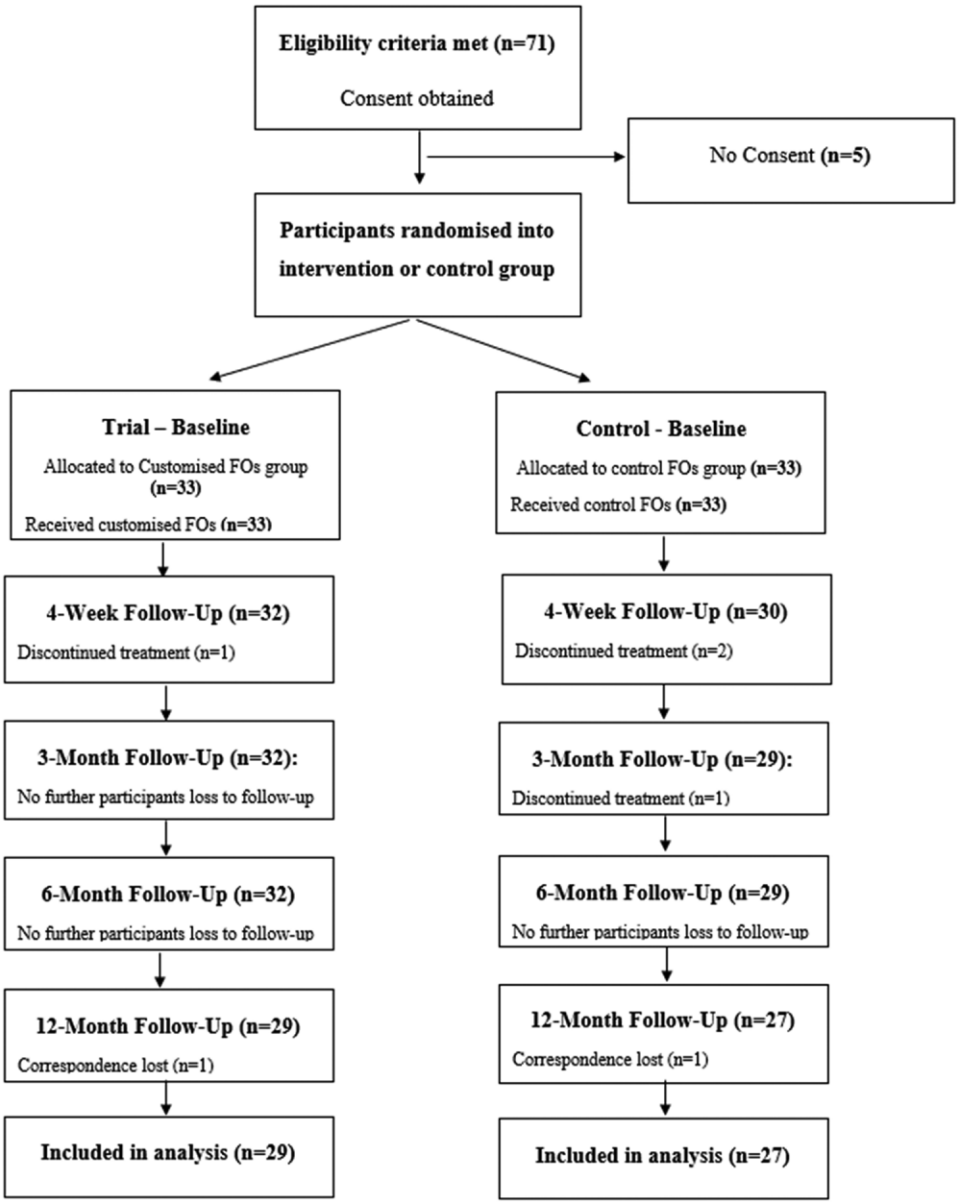

Table 2 Participant characteristics at recruitment

Participant characteristic	Trial group $n = 33$	Control group $n = 33$
Demographics		
Age, years, mean (S.D.)	11.97 (3.83)	12.09 (3.40)
Male/female, *n*	10/23	11/22
Health status		
VAS child-reported pain, mean (S.D.)	48.33 (24.07)	42.12 (26.72)
VAS parent-reported pain, mean (S.D.)	39.88 (24.82)	33.27 (24.01)
PedsQL child-reported QoL, mean (S.D.)	71.11 (16.06)	64.78 (15.04)
PedsQL parent-reported QoL, mean (S.D.)	64.08 (14.95)	59.97 (17.93)
JAFI impairment, mean (S.D.)	14.76 (7.04)	16.85 (7.55)
JAFI activity limitation, mean (S.D.)	14.73 (8.64)	16.52 (9.55)
JAFI participation restriction, mean (S.D.)	4.70 (4.16)	6.79 (3.91)
Duration of disease, years mean (S.D.)	6.70 (4.26)	6.29 (4.37)
Drug therapies		
NSAIDS, *n* (%)	6 (18)	11 (33)
Analgesics, *n* (%)	1 (3)	0 0
MTX, *n* (%)	15 (45)	17 (51)
Etanercept, *n* (%)	2 (6)	5 (15)
Adalimumab, *n* (%)	4 (12)	5 (15)
Tofacitinib, *n* (%)	1 (3)	1 (3)
Prednisone, *n* (%)	1 (3)	4 (12)
Tocilizumab, *n* (%)	4 (12)	3 (9)
SSZ, *n* (%)	1 (3)	1 (3)
Infliximab, *n* (%)	1 (3)	2 (6)
LEF, *n* (%)	2 (6)	0 0
Combination therapy-NSAID & MTX or biologic, *n* (%)	3 (9)	7 (21)
Combination therapy-DMARD & biologic, *n* (%)	5 (15)	5 (15)
ILAR subtypes		
Persistent oligoarticular, *n* (%)	4 (12)	7 (12)
Extended oligoarticular, *n* (%)	9 (27)	8 (24)
Polyarticular RF −ve, *n* (%)	9 (27)	9 (27)
Polyarticular RF +ve, *n* (%)	3 (9)	1 (3)
Psoriatic, *n* (%)	2 (6)	1 (3)
Systemic, *n* (%)	2 (6)	2 (6)
Enthesitis-related, *n* (%)	4 (12)	5 (15)
Undifferentiated, *n* (%)	0 0	0 0

ILAR: International League of Associations for Rheumatology; JAFI: juvenile arthritis foot disability index; PedsQL: pediatric quality of life; VAS: visual analogue scale.

compared with the control (mean = 44 mm, S.D. = 29.71), with a drop of 28.93 mm. This was highly clinically and statistically significant with a *P*-value of <0.001 and CIs of –40.90 mm to –16.96 mm. Six-month (trial mean = 21.77 mm, S.D. = 21.41; control mean =29.45 mm, S.D. = 23.33) and 12-month (trial mean = 29.11 mm, S.D. = 28.30; control mean = 37 mm, S.D. = 27.44) follow-ups did not reach statistical significance. Similarly to child reported pain, the parent-reported pain at 3 months follow-up produced highly statistical and clinical significance with an average reduction of 21.92 mm (trial mean = 22.61 mm, S.D. = 22.16; control mean = 42.31 mm, S.D. = 29.32) in favour of the trial group (*P*-value of <0.001 and CIs of −33.16 mm to −10.67 mm). The remaining follow-ups did not reach statistical significance, but all trends favour the trial group. Table 3 provides descriptive and statistical analysis results for all outcomes by follow-up. Supplementary Figs S1 and S2 (available at *Rheumatology* online) depict a box-and-whisker plot and line graph over time by intervention group for the child-reported pain.

Secondary outcomes

Quality of life

Quality of life measured by the PedsQL rheumatology scale did not produce statistically significant results for

TABLE 3 Descriptive and statistical analysis for pain, quality of life and foot and ankle disability from baseline to 12-months follow-up

Outcome	Trial control						
	n	mean (S.D.)	*n*	mean (S.D.)	*P*>|*z*|	Coef.	[95% CI]
Pain							
Baseline	33	48.33 (24.07)	33	42.12 (26.72)			
4-Week	32	26.81 (23.11)	30	40.97 (28.82)	0.018	−14.92	[−27.30, −2.55]
3-Month	32	16.87 (14.78)	29	44 (29.71)	<0.001	−28.93	[−40.90, −16.96]
6-Month	32	21.77 (21.41)	29	29.45 (23.33)	0.116	−9.66	[−21.72, 2.39]
12-Month	29	29.11 (28.30)	27	37 (27.44)	0.187	−8.37	[−20.81, 4.07]
Parent reported pain							
Baseline	33	39.88 (24.82)	33	33.27 (24.01)			
4-Week	32	25.27 (21.70)	30	33.93 (25.76)	0.118	−9.21	[−20.76, 2.34]
3-Month	32	22.61 (22.16)	29	42.31 (29.32)	<0.001	−21.92	[−33.16, −10.67]
6-Month	32	25.2 (22.34)	29	28.52 (20.25)	0.356	−5.41	[−16.90, 6.08]
12-Month	29	25.11 (28.50)	27	28.52 (25.43)	0.402	−5.05	[−16.86, 6.75]
PedsQL							
Baseline	33	71.11 (16.06)	33	64.78 (15.04)			
3-Month	32	73.94 (12.19)	29	67.42 (18.27)	0.598	1.51	[−4.09, 7.11]
6-Month	32	73.26 (14.80)	29	71.54 (17.85)	0.355	−2.66	[−8.29, 2.97]
12-Month	29	71.76 (16.94)	27	69.89 (19.55)	0.08	−5.23	[−11.07, 0.62]
Parent reported PedsQL							
Baseline	33	64.03 (14.71)	33	59.97 (17.93)			
3-Month	32	72.05 (14.41)	29	66.94 (20.63)	0.510	2.14	[−4.23, 8.52]
6-Month	32	69.73 (17.36)	29	71.28 (18.09)	0.257	−3.76	[−10.25, 2.74]
12-Month	29	69.32 (18.71)	27	72.77 (17.93)	0.028	−7.48	[−14.15, −0.81]
JAFI-Imp							
Baseline	33	14.76 (7.04)	33	16.85 (7.55)			
3-Month	32	9.87 (5.38)	29	13.73 (8.09)	0.095	−2.59	[−5.63, 0.45]
6-Month	32	9.23 (6.28)	29	12.52 (6.29)	0.207	−1.97	[−5.04, 1.09]
12-Month	29	11.96 (7.21)	27	11.64 (7.42)	0.147	2.36	[−0.83, 5.55]
JAFI-Act							
Baseline	33	14.73 (8.64)	33	16.52 (9.55)			
3-Month	32	8.77 (8.97)	29	13.73 (10.31)	0.07	−3.49	[−7.26, 0.28]
6-Month	32	7.71 (6.86)	29	12.62 (8.37)	0.093	−3.26	[−7.05, 0.54]
12-Month	29	10.81 (9.54)	27	12.46 (10.46)	0.489	1.38	[−2.53, 5.29]
JAFI-Part							
Baseline	33	4.70 (4.16)	33	6.79 (3.91)			
3-Month	32	3.42 (2.90)	29	5.23 (4.14)	0.231	−0.86	[−2.27, 0.55]
6-Month	32	3.19 (2.43)	29	4.17 (3.00)	0.892	−0.10	[−1.52, 1.32]
12-Month	29	4.11 (3.73)	27	5.25 (3.47)	0.936	0.06	[−1.40, 1.52]

IQR: interquartile range; JAFI-Imp: JAFI-impairment; JAFI-Act: JAFI-activity limitation; JAFI-Part: JAFI-participation restriction; *n*: number of participants; *P*>|*z*|: probability value; PedsQL: pediatric quality of life questionnaire rheumatology scale.

both child in 3-month [$P = 0.598$, 1.51 (−4.09, 7.11)]; 6-month [$P = 0.355$, −2.66 (−8.29, 2.97)]; 12-month [$P = 0.08$, −5.23 (−11.07, 0.62)] and parent in 3-month [$P = 0.510$, 2.14 (−4.23, 8.52)]; 6-month [$P = 0.257$, −3.76 (−10.25, 2.74)]; 12-month [$P = 0.028$, −7.48 (−14.15, −0.81)] reported questionnaires. The *P*-values generally showed insignificant differences and broad CIs. Interestingly, the 12-month follow-up for parent-reported PedsQL was statistically significant in favour of the control group with an average increase of 7.48 and CIs of −14.15 to −0.81.

Foot and ankle disability

Foot and ankle disability measured by the JAFI did not reach statistical significance at any follow-up or sub-scale. However, the activity limitation sub-scale of the JAFI produced *P*-values that were close to achieving statistically significant differences at 3-month ($P = 0.07$) and 6-month ($P = 0.093$) follow-ups in favour of the trial group.

Swollen and tender joints

Overall, the count of swollen joints for participants across both groups was low; therefore, only descriptive

TABLE 4 Descriptive statistics for joint swelling outcome expressed in individual and total count joint categories

Swollen	Trial				Control			
	n	Joint count	Mean (S.D.)	Median (range)	*n*	Joint count	Mean (S.D.)	Median (range)
Hip								
Baseline	33	0	0 0	0 (0–0)	33	1	0.03 (0.17)	0 (0–1)
6-Month	32	0	0 0	0 (0–0)	29	2	0.07 (0.37)	0 (0–2)
Knee								
Baseline	33	5	0.16 (0.53)	0 (0–2)	33	4	0.12 (0.48)	0 (0–2)
6-Month	32	3	0.11 (0.41)	0 (0–2)	29	1	0.03 (0.19)	0 (0–1)
Ankle								
Baseline	33	11	0.37 (0.67)	0 (0–2)	33	15	0.45 (0.71)	0 (0–2)
6-Month	32	1	0.03 (0.19)	0 (0–1)	29	18	0.62 (0.82)	0 (0–2)
STJ								
Baseline	33	5	0.17 (0.46)	0 (0–2)	33	1	0.03 (0.17)	0 (0–1)
6-Month	32	0	0 0	0 (0–0)	29	3	0.10 (0.41)	0 (0–2)
Midfoot								
Baseline	33	8	0.27 (0.83)	0 (0–4)	33	7	0.21 (0.78)	0 (0–4)
6-Month	32	3	0.10 (0.56)	0 (0–3)	29	6	0.21 (0.82)	0 (0–4)
MPJs								
Baseline	33	4	0.13 (0.43)	0 (0–2)	33	2	0.06 (0.24)	0 (0–1)
6-Month	32	0	0 0	0 (0–0)	29	1	0.03 (0.19)	0 (0–1)
PIPJs								
Baseline	33	2	0.03 (0.18)	0 (0–1)	33	1	0.03 (0.17)	0 (0–1)
6-Month	32	1	0.03 (0.19)	0 (0–1)	29	0	0 0	0 (0–0)
DIPJs								
Baseline	33	2	0.03 (0.18)	0 (0–1)	33	1	0.03 0.17	0 (0–1)
6-Month	32	1	0.07 (0.37)	0 (0–2)	29	0	0 0	0 (0–0)
Total								
Baseline	33	37	1.121 (0.98)	0 (0–8)	33	32	0.97 (1.67)	0 (0–7)
6-Month	32	9	0.47 (0.98)	0 (0–3)	29	31	1.07 (1.69)	0 (0–8)

DIPJs: 2–5 distal interphalangeal joints; Midfoot: calcaneocuboid and talonavicular joints; MPJs: 1–5 metatarsophalangeal joints; *n*: number of participants; PIPJs: 1–5 proximal interphalangeal joints; STJ: sub-talar joint.

statistics for swollen joints were provided. Poisson-regression analysis was used to detect the significance of tender joints between groups, expressed as incidence-rate ratios (IRR). The total count, ankle, sub-talar joint, mid-foot joints and MPJs were analysed. The reduction of total tender joints was not statistically significant in favour of the trial group with a *P*-value of 0.062 and an IRR of 0.49. However, the ankle and mid-foot joints were statistically significant different in favour of the trial group with *P*-values of 0.002 and 0.026, and IRRs of 0.35 and 0.19, respectively. The sub-talar joint and metatarsophalangeal joints were not statistically significantly different. Further descriptive statistics for joint swelling and tenderness are available in Tables 4 and 5, respectively.

Adherence to intervention and participant withdrawals

Results from the FOs diary showed the average days per week participants in the study wore their FOs was 4.55 days. The trial group wore their FOs 0.3 days longer at 4.7 days per week, *vs* the control at 4.4 days. Overall, five participants in the control group withdrew: three discontinued treatment as they reported discomfort wearing their FOs; two participants failed to return their surveys and were non-responsive to communication attempts. Two participants in the trial group withdrew: one participant discontinued treatment as they reported discomfort wearing their FOs; one participant withdrew as they failed to return their surveys and were non-responsive to communication attempts.

Medication changes

Information on medication changes are presented in Supplementary Table S2, available at *Rheumatology* online.

Success of blinding participants

Parents and participants were asked if they were aware of their group allocation at any stage during the clinical trial. Fifty-six participants and parents were asked in which 95% stated that they were not aware of what group they were randomized to. Only three participants were seemingly aware of their intervention as their answers to what group they were allocated were correct.

Trial group customizations. Supplementary Table S3 (available at *Rheumatology* online) depicts the results of the customizations prescribed to participants in the trial group. Twenty-five of the 33 participants in the trial

Table 5 Descriptive and statistical analysis for joint tenderness outcome expressed in individual and total count joint categories

Tender	Trial				Control						
	n	Joint count	Mean (s.d.)	Median (range)	*n*	Joint count	Mean (s.d.)	Median (range)	IRR	*P*>|*z*|	[95% CI]
Hip											
Baseline	33	0	0 0	0 0	33	1	0.03 (0.17)	0 (0–1)			
6-Month	32	0	0 0	0 0	29	2	0.07 (0.37)	0 (0–2)			
Knee											
Baseline	33	7	0.21 (0.60)	0 (0–2)	33	7	0.21 (0.60)	0 (0–2)			
6-Month	32	5	0.17 (0.51)	0 (0–2)	29	4	0.14 (0.44)	0 (0–2)			
Ankle											
Baseline	33	41	1.24 (0.75)	1 (0–2)	33	34	1.03 (0.85)	1 (0–2)			
6-Month	32	12	0.38 (0.71)	0 (0–2)	29	31	1.07 (0.88)	1 (0–2)	0.35	0.002	[0.18, 0.68]
STJ											
Baseline	33	20	0.61 (0.86)	0 (0–2)	33	10	0.30 (0.64)	0 (0–2)			
6-Month	32	6	0.19 (0.54)	0 (0–2)	29	9	0.31 (0.66)	0 (0–2)	0.60	0.457	[0.16, 2.82]
Midfoot											
Baseline	33	22	0.67 (1.36)	0 (0–4)	33	13	0.39 (0.93)	0 (0–4)			
6–Month	32	4	0.13 (0.34)	0 (0–1)	29	19	0.66 (1.32)	0 (0–4)	0.19	0.026	[0.04, 0.82]
MPJs											
Baseline	33	17	0.50 (0.97)	0 (0–3)	33	7	0.21 (0.89)	0 (0–5)			
6-Month	32	3	0.10 (0.41)	0 (0–2)	29	5	0.17 (0.60)	0 (0–3)	0.60	0.484	[0.14, 2.5]
PIPJs											
Baseline	33	1	0.03 (0.17)	0 (0–1)	33	0	0 0	0 (0–0)			
6-Month	32	4	0.13 (0.71)	0 (0–4)	29	0	0 0	0 (0–0)			
DIPJs											
Baseline	33	1	0.03 (0.18)	0 (0–1)	33	0	0 0	0 (0–0)			
6-Month	32	4	0.13 (0.71)	0 (0–4)	29	0	0 0	0 (0–0)			
Total											
Baseline	33	109	3.30 (3.02)	2 (0–12)	33	72	2.18 (2.14)	2 (0–8)			
6-Month	32	38	1.19 (2.43)	0 (0–10)	29	70	2.41 (2.63)	2 (0–11)	0.49	0.062	[0.23, 1.04]

DIPJs: 2–5 distal interphalangeal joints; IRR: incidence-rate ratio; Midfoot: calcaneocuboid and talonavicular joints; MPJs: 1–5 metatarsophalangeal joints; *n*: number of participants; *P*>|*z*|: probability value; PIPJs: 1–5 proximal interphalangeal joints; STJ: sub-talar joint.

group were prescribed two customizations based on the study's protocol [20]. The most commonly prescribed combination was a 3.5 or 5-degree antipronatory wedge with a valgus arch dome to increase midfoot contact and/or reduce excessive midfoot pronation.

Adjusted analysis. To determine whether changes of medication and disease status impacted on the results, an adjusted analysis was conducted. Participants who experienced joint or disease flares causing a changes of medications during their 12-month involvement in the clinical trial were removed from a sub-group analysis. Two changes were seen in the child-reported pain outcome: the 4-week follow-up became not statistically significant in favour of the trial group with a *P*-value of 0.075 and CIs of −25.85, 1.25; while the 6-month follow-up changed from being not statistically significant to statistically and clinically significant in favour of the trial group with a *P*-value of 0.03 and CIs of −27.84 to −1.45. Parent-reported PedsQL at 12 months ($P = 0.131$, CIs −13.94, 1.81) and tender midfoot joints ($P = 0.06$, CIs, 0.06, 1.29) with an adjusted analysis produced non-statistically significant results. Finally, while it did not change the status of statistical significance, child-reported pain at 12-month follow-up was close to achieving statistical and subsequently clinical significance. The average reduction in pain in favour of the trial group was −13.13 mm with a *P*-value of 0.06 and CIs of −26.80, 0.53.

Discussion

Primary outcome

In this study, customized preformed FOs were chosen as the trial intervention as they are able to be prescribed on the same day of the initial consultation, are inexpensive (average cost A$30) and safe to use in a paediatric population. Results indicate customized preformed FOs are effective in reducing short- to medium-term pain in children with JIA. At 4 weeks, pain in the trial group reduced on average by 14.92 mm, then 28.93 mm at 3 months compared with the control group. 28.93 mm reduction in pain after 3 months is remarkably clinically significant, given the minimal important clinical difference is 8 mm. Both participant and parent perceptions of pain were highly statistically and clinically significant at the 3-month follow-up, indicating a rapid and significant clinical effect of customized preformed FOs in the reduction of pain in children with symptomatic lower limb arthritis. These results are consistent with Coda *et al.* (2014), who also detected significant reductions in pain using a similar intervention [14]. This intervention is also clinically effective in reducing pain only 4 weeks after fitting the device. Despite significant reductions in pain at the 4-week and 3-month follow-ups, this was not detected at the 6- and 12-month intervals in both child and parent pain reporting. Effect sizes sharply dropped after 3 months of the intervention; therefore, clinicians may need to monitor the usage of the FOs and review the prescription regularly to promote sustained efficacy.

Secondary outcomes

PedsQL reports from both children and parents were insignificant, indicating the trial intervention did not have an impact on health-related quality of life. The control group did show to have statistically and clinically significant improvements in PedsQL at the 12-month follow-up *vs* the trial group. However, a sub-group analysis accounting for medication-changed participants produced statistically insignificant results for this outcome. The trial intervention did not statistically or clinically reduce foot and ankle disability measured by the JAFI. This includes all follow-ups and sub-scales which is also consistent with another podiatric-based RCT in children with JIA [15]. The prevalence of joint swelling in participants across both groups was relatively low; therefore, the statistical effect of customized preformed FOs on joint swelling remains unclear. Data for swelling showed the count in the control group remained virtually the same, while the total count for swollen joints in the trial group reduced by 75% from baseline to the 6-month follow-up. The comparison of the total tender joint count between trial and control groups was not statistically significant ($P = 0.062$). Descriptively, the total tender joint count reduced by 75% in the trial group, while the control group's total tender joint count remained the same at the 6-month follow-up. The ankle and midfoot joints produced statistically significant differences in favour of the trial group post intervention. The ankle and midfoot joints produced IRRs of 0.35 and 0.19 and were 65% and 81% less likely to have a tender ankle and midfoot joint 6 months post intervention, respectively. This suggests customized preformed FOs are effective in reducing tender ankle and midfoot joints in children with JIA. This is consistent with the primary outcome results in this clinical trial with participants in the trial group perceiving statistically and clinically significant less pain than control participants.

Limitations

First, the results of this clinical trial reflect findings from a specific preformed device and may not be generalisable to other preformed or prefabricated FOs. Changes in pain may not be fully attributed to the intervention because JIA is subject to fluctuations in global disease activity, which was not measured in this study. Adjusted analysis indicates changes to medication and disease status during participants' 12 months of involvement may have impacted on the validity of results. Child-reported pain results appeared to be affected the most when medication-changed participants were removed in a sub-group analysis. Despite some changes in significance of the primary outcome with an adjusted analysis, strong trends leaned in favour of the trial group. For example, the 12-month follow-up for child-reported pain

was almost statistically significant with an average reduction of −13.13 mm of pain and a *P*-value of 0.06. Ultrasound examination for swollen joints would have increased diagnostic accuracy and validity of findings. Seven participants were lost at various stages throughout the trial. Only one participant in the trial group withdrew due to discomfort with their FOs. They reported the presence of blistering shortly after wearing them and opted to withdraw from the study. This was the only case of an adverse albeit minor event with the trial intervention.

Clinical implications and directions for future research

In summary, clinicians managing children with JIA can use customized preformed FOs to reduce lower limb pain and tenderness of ankle and midfoot joints. Clinicians should expect pain to reduce within a month post prescription and to continue reducing for least 3 months. The long-term effect of FOs in reducing lower limb pain and swollen lower limb joints in children with JIA remains unclear. JIA is a chronic disease; therefore, future research may explore the effect that FOs have on managing long-term lower limb problems in JIA beyond 12 months. While customized preformed FOs have shown to be effective in the short and medium term in JIA, there are no clinical trials that have directly compared custom-made FOs verses customized preformed FOs in both long-term cost-effectiveness and durability.

Conclusion

This clinical trial has shown that customized preformed FOs are statistically and clinically significant in reducing lower limb pain in children with JIA during the first 3 months of intervention. Significant reductions in pain were not sustained beyond 3 months. Customized preformed FOs were also statistically significant in reducing joint tenderness in the ankle and midfoot. The impact of FOs on swollen joints and overall disease activity remains unclear. Overall, the FOs used in this clinical trial were inexpensive, easy to dispense and well tolerated by participants with virtually no adverse events. Finally, paediatric rheumatology team members may prescribe the proposed intervention to reduce lower limb and particularly foot and ankle pain in children and adolescent with JIA. The tested intervention has the potential to be easily accessible by patients, affordable to the public health system and rapidly translated to the podiatry and paediatric rheumatology community.

The Hunter New England Human Research Ethics Committee approved this clinical trial (reference number: 16/09/21/4.03). Site authorisation was also approved for all data collection sites by the relevant research governance committees.

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All authors contributed to the overall design of the study. D.S.-G. and J.C. were responsible for identifying potentially eligible participants, and A.F. recruited them in the trial. A.F. was responsible for all face-to-face research visits for participants. A.C. conducted sequence generation and allocation concealment. M.C. was the biostatistician for this clinical trial and was responsible for designing the statistical analysis. All authors drafted the manuscript, critically revised the article for important intellectual content, and provided final approval of the submitted version.

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Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

Supplementary data

Supplementary data are available at *Rheumatology* online.

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