The clinical and cost-effectiveness of foot orthoses in people with established rheumatoid arthritis: an exploratory clinical trial

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ABSTRACT

Objectives: Foot orthoses are commonly prescribed as an intervention for people with rheumatoid arthritis. The aim was to evaluate the clinical and cost analysis of two foot orthoses in people with established rheumatoid arthritis.

Methodology: A single-blind randomised controlled trial was undertaken to compare customised foot orthoses and simple insoles in 41 people with established rheumatoid arthritis. The Foot Function Index measured foot pain, disability and functional limitation. Costs were estimated from the perspective of the NHS and from the societal (patient and family) perspective to include costs from outside the NHS. Effects were assessed in terms of health gain expressed as quality adjusted life years (QALYS).

Results: At baseline, 20 participants received the customised foot orthoses and 21 participants received a simple insole. After 16 weeks foot pain improved for both the custom-made foot orthoses (p=0.000) and simple insoles (p<0.01). Custom-made foot orthoses improved disability scores (p<0.001) but not for simple insoles (p=0.40). The cost effectiveness results demonstrated no difference in cost between the arms (custom-made foot orthoses: £159.10; simple insole: £79.10 p=0.35), with the customised foot orthoses being less effective in terms of cost per QALY gain (p<0.001).

Conclusions: In people with established RA, semi-rigid customised foot orthoses can improve pain and disability scores in comparison to simple insoles. From a cost effectiveness analysis perspective the customised foot orthoses were far more expensive to manufacture, with no significant cost per QALY gain.

Keywords: rheumatoid arthritis, foot orthoses, cost-analysis, foot pain, foot impairment

INTRODUCTION

Rheumatoid arthritis (RA) can lead to rapid development of joint damage and significant long-term disability [1]. Over 75% of RA patients report foot involvement within four years of diagnosis, and the reported prevalence of foot problems is as high as 50–90% [2-5]. Progressive joint destruction leads to varying degrees of physical disability with over 70% of all individuals with RA reporting moderate to severe foot pain, exposing a significant clinical challenge and an international public health priority [6].

Clinically effective management of foot pain and prevention of foot deformity are the chief goals of intervention for people with RA [6,7]. Non-pharmacological interventions for RA that include foot orthoses and footwear can reduce pain and disability and improve long-term outcomes with existing and potential foot problems [8, 9]. Previous studies have reported on the clinical effectiveness of foot orthoses in people with established RA [10-13]. The National Institute for Clinical Effectiveness (NICE) reported the estimated annual cost of RA to be between £3.8 and £4.75 billion per year, including direct costs to the UK National Health Service (NHS) and other healthcare support agencies and indirect costs to the economy, including productivity losses and the personal impact on RA patients and their families [14]. Clark [15] reported that few studies have undertaken a cost effectiveness analysis to investigate the cost implication of the prescription of foot orthoses for people with foot pain and established RA, despite the high prevalence of foot involvement and the high direct cost of RA related health care to the UK economy. The issue of the cost effectiveness of providing foot orthoses in the NHS has been raised in chronic musculoskeletal foot conditions [16], as it represents a considerable burden to patients, clinicians and health providers. However, data relating to cost-effectiveness of the use of foot orthoses in people with RA are limited (17,18). With such limited data the aim of this study was to evaluate the clinical and cost analysis of custom-made foot orthoses compared to simple insoles when prescribed for people with established RA.

METHODOLOGY

The research design was a single-blinded, exploratory randomised controlled clinical trial conducted over 16 weeks with participants randomly assigned to two intervention arms: custom-made foot orthoses (CMFO) or simple insoles (SI). The study design according to the CONSORT statement is demonstrated in Figure 1 [19]. Participants were recruited from a rheumatology outpatients department in the North-East of England, UK. Participants were eligible if they were over 18 years

old, history of foot pain, ability to walk a required distance of 5m for measurement of foot function and had a diagnosis of RA according to the American College of Rheumatology/European League Against Rheumatism revised criteria [20]. Participants with a history of previous foot surgery or ulceration, those with an unstable medical regime or in a state of flare, currently using foot orthoses or unwilling to change their footwear to accommodate an orthotic, or with poor language ability or inability to understand the research protocol were excluded. Local ethical approval was obtained from Teesside University. All participants gave informed consent to participate in the study. The trial was registered with ANZCTR (ACTRN12615001252505).

Sample size estimates for use in the study were calculated using sample size calculation tables [21]. For a large effect size (d) of 0.8, it was calculated that the trial would require 20 participants per arm to detect arm differences with 80% power. A plan for allocating to either intervention arms was independently generated using randomisation software available from St George's Hospital Medical School website, http://www.sgul.ac.uk/depts/chs/chs_research/stat_guide/guide.cfm. Participants were recruited by the primary researcher and once baseline data had been collected the primary researcher contacted the independent investigator for arm allocation. Participants were blinded to the intervention.

Participants were randomly allocated to receive either CMFO or SI. The CMFO were manufactured from high density ethyl vinyl acetate, with a thickness of 20mm and a shore density of 50, a contoured medial arch, high heel cup and external medial posting correction customised to each patient according to the amount of valgus rearfoot deformity present and maximum forefoot balancing technique, determined by the external manufacturer providing the interventions (Langer Biomechanics Arm, Cheadle, UK). Both foot orthoses were covered with 1.6mm cushioning material extending the length of the foot. The SIs were a simple 6mm cushioning insole made from a breathable foam core on a rubber-silicone-ethylene compound, cut to fit the exact shape of the participants' footwear. Both interventions used the same top colour.

At the baseline visit age, sex, ethnicity, clinical characteristics and current pharmacological management were recorded. Foot disease impact was measured using the Foot Function Index [22]. The Foot function Index is a self-administered questionnaire consisting of 23-items armed in three

domains: foot pain (nine items), disability (nine items) and functional limitation (five items). Higher scores indicate greater pain, disability and limitation of activity and thus poorer foot health.

PROCEDURE

A neutral suspension plaster of Paris cast was taken of participant's feet to enable provision of the CMFO. Participant's footwear was evaluated to ensure footwear was suitable to accommodate either foot orthoses. A template was taken to determine shoe size. These activities were timed to aid in the evaluation of cost effectiveness and further information regarding cost effectiveness was collected. Randomisation allocation to either CFMO, made from the neutral suspension casts, or the SI, which were cut to fit the patients' shoe was undertaken. To record weekly wear time and adverse events, which occurred during the 16-week study period, participants were issued with diary at the baseline study visit.

We conducted a cost utility analyses which addresses health related quality of life. NICE in England has recommended the use of quality-adjusted life years (QALYs) as the measure of health benefit for economic analysis as it allows comparisons across different clinical conditions, unlike condition specific quality of life measures [23]. We estimated costs from a NHS and from the NHS and patient perspective. We micro-costed NHS secondary care resource use in terms of the intervention and staff time spent with the participant via a healthcare personal proforma completed at baseline and 16 weeks follow up. Costs to participants in terms of out of pocket expenses and travel costs were estimated by a health economics patient self-completed proforma at baseline and 16 weeks. We derived unit costs of these sources from various sources [24] for podiatrists time (unit cost per minute for Band 5: 0.53). We obtained the costs of the foot orthoses (unit cost: £ 68.32) and the simple insole (unit cost of £24.82) to the NHS from Langer UK Ltd. Out of pocket and travel expenses incurred by participants were inflated to 2015 prices using the retail price index [25].

We estimated the effects on health related quality of life (utilities) of the interventions and undertook a cost-utility analysis using QALYs as the measure of effect. We estimated participant utilities by administering the EQ5D instrument [26] at baseline and 16 weeks; combined them with the area under the curve method to calculate QALY gains over the 16 week study period; and corrected for baseline EQ5D. We estimated the cost per QALY gain by dividing differences in cost by differences in QALYs and compared by the thresholds recommended by NICE [23].

Data Analysis

We analysed data in SPSS version 22.0 (SPSS Inc., Chicago II, USA) and MS Excel 2010 (Microsoft Corporation, Redmond, Washington DC, USA). Results were reported according to the CONSORT statement [27]. All descriptive data and health status measurements were obtained at baseline and 16 weeks. All participant data was included in the final data analysis to ensure continuity of balance in both arms of the trial to reduce bias. All data was subjected to tests for accuracy and quality before analysis was undertaken. No transformation of data was undertaken. Differences between the two arms were determined by analysis of covariance (ANCOVA), to assess the impact of the two different FO interventions on participants' scores across the time periods of the trial. Where appropriate, as when dealing with categorical data, non-parametric tests such as Mann Whitney U tests were used. R (R-Foundation for Statistical Computing, Vienna, Austria) and Statistical Analysis Software (SAS Institute Inc) using the sub-heading Proc Mixed for the ANCOVA. Differences between and within arms were presented as mean differences and 90% confidence intervals (90%CI). This has been recommended as an appropriate confidence level and also as a way of discouraging reinterpretation of the 90%CI as significant or non-significant at the 5% level [28]. Because of the small numbers of participants in our trial we performed boot-strapped t-tests to estimate the differences between utilities at each of the three time points and report means and standard deviations of the boot-strapped samples. To estimate effects on QALYS, we performed a linear regression with QALY gain as the dependent variable with treatment arm and baseline utility as independent variables. The level of statistical significance was set at 0.05.

RESULTS

One hundred and twenty participants were identified as potential participants in the study and forty-one participants were randomised. The majority of participants were females (n=28, 68%) with a mean (SD) of 62 (10) years old and a mean (SD) disease duration of 14 (9) years. All participants were receiving NSAIDS (n = 36, 88%) and DMARDS (n = 37, 90%). At baseline, 20 participants received the CMFO and 21 participants received the SI. At 16 weeks, 75% (n=15) of participants in the CMFO-arm and 66% (n= 14) participants in the SI-arm completed the study. Twelve participants (29%) withdrew over the course of the study (Figure 1).

Table 1 demonstrates the descriptive statistics for the Foot Function Index domains. All participants wore their FOs when attending for review and reported wearing them in the week prior to review. The two interventions were worn on average 77 hours/week (CMFO-arm with an average of 87 hours and the SI-arm an average of 67 hours). Three participants reported initial fit problems related to the thickness of the shoe insert, two withdrawing and one continuing within the trial after modifying footwear to increase the depth to accommodate the CMFO. No other adverse reactions were recorded. There was no difference between the two arms in wearing times over the 16 weeks (p=0.60). Table 2 demonstrates the differences between the sub-domains of the Foot Function Index from baseline to 16 weeks. The pain score reduced significantly in both intervention arms (p<0.000). The treatment effect of the intervention at 16 weeks was not significant between the two arms (p = 0.14). The reduction in foot disability score was significant in the CMFO arm (p<0.000), but not in the SI arm (p =0.40). The treatment effect at 16 weeks did not reach significance (p = 0.12). The change in the activity limitation score did not reach significance in both arms (p<0.05).

The effects of the interventions on health related quality of life (utility) and QALYs are shown in Table 3. At baseline there was a, statistically insignificant difference between the arms of the trial. The difference in baseline utility was 0.10 in favour of the CFMO-arm. The CFMO-arm showed a decrease in utility at 16 weeks compared to baseline whereas the SI-arm showed an increase. When the area under the curve controlling for baseline utility method was applied, there was small statistically insignificant QALY loss associated with the CFMO intervention compared to SI. Therefore there no statistically significant effect of the intervention on QALYs was found.

The frequency of podiatric staff time was similar for both interventions at baseline and both follow-up periods (Table 4). Across the two-arms of the trial, the only significant difference in costs was that the CFMO being more expensive than the SI with a mean difference of £8.53 (bootstrapped 90% CI: £8.53 to £8.53). This lead to a statistically significant difference in total costs to the NHS with a mean difference of £8.90 (bootstrapped 90% CI: £5.02 to £13.27). The mean costs of resource use over the 16 week follow-up period are illustrated in Table 5. The mean health gain, expressed as a difference in mean QALYs between interventions over the 16 week follow-up period, was -0.03 and the difference in mean cost to the NHS was £8.90. From either costing perspective (NHS alone or

NHS & patient), the CFMO was both more expensive and less effective than the SI and is therefore dominated.

DISCUSSION

NICE have suggested that interventions delivering a cost per QALY of under £20,000 are likely to be an acceptable use of NHS resources [17]. The current findings support the notion that foot orthoses for people with established RA delivers a cost-effective intervention. In both arms, from the societal perspective, patients' costs were approximately equal and no further sensitivity analysis was undertaken. The cost per QALY gain results found in this study would suggest that the average cost per QALY gain is less than the NICE threshold and is therefore, an acceptable use of NHS resources. The main analysis was undertaken using only 16 weeks data, although it is likely that any benefits achieved within this period would be maintained for a longer period of time. It is plausible that changes in costs could have occurred over a longer time frame than the 16-week period, but this is an assumption without evidence therefore it was considered reasonable to assume equally distributed costs for this study. Both arms also only showed minimal improvement over the course of the study, but this may reflect a lack of sensitivity of the EQ5D to pick up subtle disease changes in the RA foot, which may have been masked by overall disease activity.

We did find that pain scores improved significantly in both the arms, with a significant improvement in both the disability domain and total Foot Function Index scores for the CMFO-arm. We found that there is a significant difference in cost between the two arms. The major difference in cost between the two arms maybe explained in terms of manufacturing time and costs of materials used in the manufacturing process with the CMFO costing significantly more to produce. However, the CMFO only produced some benefit in terms of patient outcomes. From a cost effectiveness analysis perspective the CMFO evaluated were far more expensive to manufacture, with the CMFO being £52.60 more expensive than the SI from an NHS perspective and £80.00 more expensive from an NHS and societal perspective. The CMFO may therefore be considered unlikely to be cost effective in comparison with the SI in the treatment of this cohort of RA patients of more than 2 years duration with foot pain, although still an acceptable use of healthcare resources overall. This does contrast with the cost-effectiveness study by Rome [16] which found that semi-rigid prefabricated foot orthoses resulted in a better quality of life for patients with plantar heel pain, despite being more

expensive. It is, however, difficult to make any further comparisons with this study as the participant arm investigated was heterogeneous. The current study should therefore call into question the use of CMFO in preference to SIs in people with established RA, although further research would be needed to make any definitive recommendations.

The current findings do present ramifications for health care professionals prescribing foot orthoses in people with established RA. A technology appraisal of foot orthoses has also not yet been undertaken by NICE, and although both interventions are likely to both deliver a cost per QALY of under £20,000 this finding does indicate that further research is necessary to support the prescription of foot orthoses in this cohort of patients as being both cost and clinically effective. The sample size used for this study also limits validity as modelling was unable to be undertaken as a result, but as there is limited economic studies to draw upon in foot orthoses evidence which can knowledgably inform public health policy either locally or nationally. The current study relates to people with established RA, therefore future work could include cost effectiveness studies evaluating to the use of foot orthoses with early RA or in other inflammatory conditions. The current study was also undertaken using participants from the North-East of England, and therefore cannot be generalizable to all people with established RA. This study looked at the cost analysis of CMFO and SI and did not consider prefabricated foot orthoses. A larger clinical trial could be undertaken to investigate the cost effectiveness of simple insoles in people with established RA and further investigation into the cost effectiveness of foot orthoses in people with early RA.

CONCLUSION

The exploratory trial was novel as it has undertaken the cost effectiveness evaluation of the use of customised foot orthoses and simple insoles in people with established RA. Future research should be undertaken to evaluate the cost effectiveness of these devices in large scale studies involving both newly diagnosed and established people with RA, clearly defining the different types of foot orthoses to investigate and within different disease durations, with the aim to make recommendations regarding clinical provision and an acceptable cost ratio to provide foot orthoses. This will further inform health care professionals but may also stimulate discussion at higher levels and highlight the need for policy makers such as NICE to undertake Technology Appraisals and further assess interventions which are less invasive.

Conflict of interest

All authors declare there are no conflicts of interests.

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Table 1: Descriptive statistics for the Foot Function Index domains

Variables	Custom Made Foot Orthoses Mean (SD)	Simple Insoles Mean (SD)
Foot Pain		
Baseline	54.2 (14.2)	54.7 (23.4)
16 weeks	30.8 (22.1)	41.3 (17.9)
Foot Disability		
Baseline	53.3 (21.5)	51.1 (19.0)
16 weeks	38.8 (24.2)	33.7 (27.1)
Functional Limitation		
Baseline	28.2 (25.3)	17.8 (11.8)
16 weeks	22.8 (17.4)	17.4 (11.7)

Table 2: Differences of Foot Function Index sub-domains from baseline to 16 weeks

Variables	Mean Difference between baseline and 16 weeks (90%CI)	P
Foot Pain		
Custom Made Foot Orthoses	-23.1 (-30.9 to -15.2)	<0.000
Simple Insole	-12.9 (-21.0 to -4.8)	0.01
Treatment effect	-10.2 (-21.5 to 1.3)	0.14
Foot Disability		
Custom Made Foot Orthoses	-16.3 (-25.8 to -6.9)	0.00
Simple Insole	-3.9 (-12.9 to 5.2)	0.40
Treatment effect	-12.4 (-25.5 to 0.6)	0.12
Functional Limitation		
Custom Made Foot Orthoses	-1.1 (-6.5 to 4.4)	0.74
Simple Insole	0.2 (6.4 to -6.8)	0.95
Treatment effect	-1.3 (-10.0 to -7.4)	0.80

Table 3: EQ5D utility index at baseline and 16 weeks

Outcome	Bootstrapped Mean (SD)		Estimated Difference. Adjusted for Baseline (90% CI)	P
	Custom Made Foot Orthoses	Simple Insole		
Baseline utility	0.59 (0.07)	0.49 (0.32)	0.10 (-0.08 0.26)	0.34
16 Weeks utility	0.57 (0.28)	0.56 (0.22)	0.01 (-0.15 0.14)	0.94
QALY	0.04 (0.10)	0.00 (0.10)	-0.03 (-0.08 0.03)	0.46

Table 4: Mean NHS Resource Use

Podiatrist Time Spent with Participant (minutes)	Custom Made Foot Orthoses Mean (SD)	Simple Insole Mean(SD)
Time spent at baseline	24 (5)	23(7)
Time spent at 16 weeks	20 (8)	20 (3)

Table 5: Mean cost of resource use (£) over the 16 week follow-up period

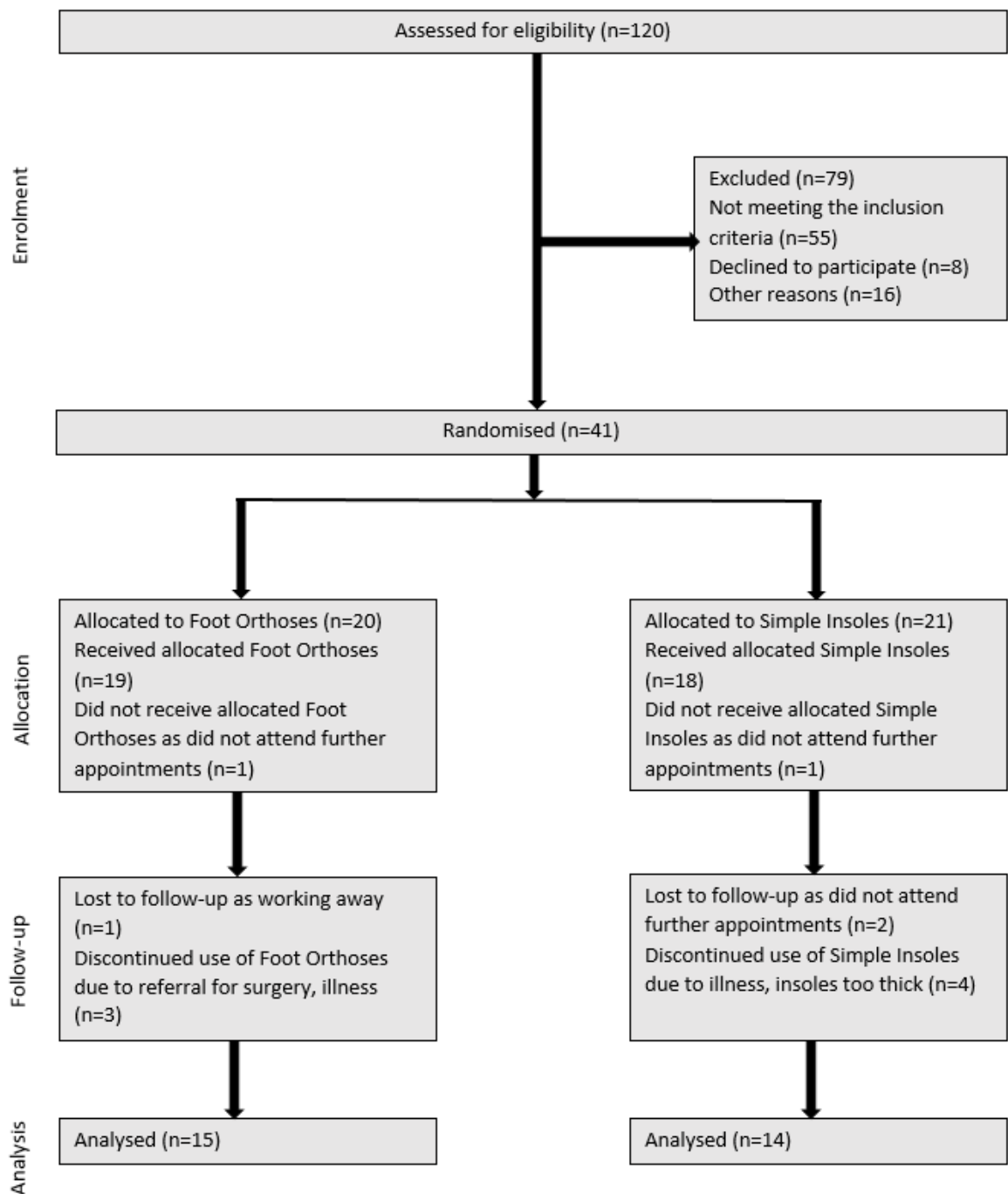| Resource Use	Custom Made Foot Orthoses Mean (SD)	Simple Insole Mean (SD)	Mean difference (90% CI bootstrapped)
Cost of intervention	33.35 (0)	24.82 (0)	8.53 (8.53,8.53)
Total podiatrists time	33.25 (7)	32.78 (7)	0.46 (-3.54, 4.70)
Total costs of equipment purchased by participants	20.24 (47.46)	9.38 (25.30)	10.85 (-10.40, 35.79)
Total costs of journeys	11.21 (9.52)	7.45 (6.15)	3.76 (-0.60, 8.77)
Total Costs to participants	31.45 (50.15)	16.86 (28.02)	14.62 (-8.27,40.53)
Total Costs to the NHS (podiatrists time plus intervention cost)	76.56 (7.07)	67.66 (6.75)	8.90 (4.78,13.39)
Total costs to the NHS and participants	108.01 (55.42)	84.50(29.30)	23.52(-1.67,50.94)

Figure 1: CONSORT flow chart