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REVIEW ARTICLE

A systematic review and narrative synthesis of footwear and orthotic devices used in the management of ankle haemarthrosis and haemarthropathy in haemophilia

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Abstract

Introduction: Haemarthrosis is a clinical feature of haemophilia leading to haemarthropathy. The ankle joint is most commonly affected, resulting in significant pain, disability and a reduction in health-related quality of life. Footwear and orthotic devices are effective in other diseases that affect the foot and ankle, such as rheumatoid arthritis, but little is known about their effect in haemophilia.

Aims: To review the efficacy and effectiveness of footwear and orthotic devices in the management of ankle joint haemarthrosis and haemarthropathy in haemophilia.

Methods: A systematic literature review was conducted. Two review authors independently screened studies for inclusion and appraised methodological quality using Joanna Briggs Institute Critical Appraisal checklists. A narrative analysis was undertaken.

Results: Ten studies involving 271 male participants were eligible for inclusion. All studies were quasi-experimental; three employed a within-subject design. Two studies included an independent comparison or control group. A range of footwear and orthotic devices were investigated. Limited evidence from non-randomised studies suggested that footwear and orthotic devices improve the number of ankle joint bleeding episodes, gait parameters and patient-reported pain.

Conclusion: This review demonstrates a lack of robust evidence regarding the efficacy and effectiveness of footwear and orthotic devices in the management of ankle joint haemarthrosis and haemarthropathy in haemophilia. Methodological heterogeneities and limitations with the study designs, small sample sizes and limited follow-up of participants exist. Future studies utilising randomised designs, larger sample sizes, long-term follow-up and validated patient-reported outcome measures are needed to inform the clinical management of ankle joint haemarthrosis and haemarthropathy.

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KEYWORDS
ankle, footwear, haemarthrosis, haemophilia, orthotic devices

1 | INTRODUCTION

Haemarthrosis, whereby bleeding occurs within a joint, is a hallmark feature of severe and moderate (bleeding phenotype) haemophilia.[1] A single episode of haemarthrosis can trigger a biological process that leads to joint synovitis and cartilage damage in the short term, and with significant or repeated minor episodes of haemarthrosis leading to the longer term development of haemarthropathy.[2,3] The use of primary and secondary prophylaxis regimes with standard half-life clotting factor products has led to a decline in the incidence of haemarthrosis, whilst the introduction of novel factor and non-factor treatments have reduced annual bleed rates and annual joint bleed rates further.[4–7] Despite this improvement in pharmacological management some patients continue to develop multi-joint haemarthropathy, resulting in significant levels of pain and decline in health-related quality of life (HRQoL).[8,9]

Historically, the knee was most frequently affected by haemarthrosis and haemarthropathy; however, following the introduction of prophylaxis therapy the ankle has become the most common site of bleeding and joint health decline.[10] It is not fully understood why this change has occurred, but it is thought to be related to increased levels of activity combined with high compressive and shearing forces at the ankle during joint loading.[11] Foot deformities occurring as a result of haemarthropathy include fixed plantarflexion, rearfoot valgus and pes planus.[12] A reduction of up to 80% in ankle range of motion (ROM) has been reported by the third decade of life, resulting in significant pain and disability.[13,14] People with Type 3 von Willebrand disease (VWD) can also develop haemarthropathy following haemarthrosis, with similar outcomes.[12,15]

In-shoe orthoses, casted insoles, functional foot orthoses, stirrup, braces and ankle foot orthoses describe devices that exert, change or redistribute forces and pressure at the shoe foot interface.[16,17] They are made of a variety of materials, ranging from rigid carbon fibre to softer cushioning foams, and aim to improve pain, comfort and stabilise the foot and ankle joint in the presence of pathology. Where the functional ankle ROM is impeded by pathological change, use of modified footwear with adaptions such as a rocker sole unit have been shown to facilitate loss of movement and protect joint margins from soft tissue impingement and associated pain.[18–20] In the presence of pathology where ankle ROM is limited, use of a combination of orthotic devices and modified footwear can reduce potential anatomical stress and supplement the rocker function of the ankle, allowing forward progression during gait.[21,22]

In other diseases affecting the ankle joint, such as inflammatory arthritis (IA) and osteoarthritis (OA), there is emerging evidence relating to the use of footwear and orthotic devices.[20,23] These interventions have been shown to prevent foot deformity, reduce patient-reported pain and disability, and improve quality of life.[16,24,25] The links between ankle haemarthropathy and pain, changes in joint structure and function, and abnormal biomechanics are well established.[26] Despite this, evidence for the use of footwear and orthotic devices in managing this condition has not been sufficiently explored, there are currently no clinical guidelines relating to which devices should be prescribed, or when a device should be utilised in clinical practice.[27–30]

The aim of this review, therefore, was to summarise and synthesise the current evidence for the efficacy and effectiveness of footwear and orthotic devices in the management of ankle haemarthrosis and haemarthropathy in haemophilia.

2 | MATERIALS AND METHODS

2.1 | Protocol

The protocol was registered with PROSPERO (registration number CRD4201914229). Reporting is in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[31]

2.2 | Eligibility criteria

Quantitative or qualitative studies evaluating the use or acceptability of footwear and orthotic device interventions were included. We included full, peer-reviewed papers only (no conference abstracts), and our search was limited to publications in the English language. There were no other exclusions on the study type.

Studies with participants aged 0–85 years old and a diagnosis of mild, moderate or severe haemophilia (A or B) or VWD type 3, and ankle haemarthrosis and/or ankle haemarthropathy were included, as haemophilia studies typically include a combined adult and child population.[32] There were no restrictions on study setting or country. Studies with participants with a diagnosis of VWD type 1 or type 2, or any other bleeding disorder were excluded.

Studies investigating any footwear and/or orthotic device interventions were included. We defined orthotic devices as ankle-foot orthoses (AFO), footwear, braces, and foot orthoses (FO). As all types of studies were eligible for inclusion, no specific concurrent comparator was required. There were no restrictions on outcome measures.

2.3 | Search strategy and study selection

Our search strategy was developed with input from an information scientist (JCE). Search terms are presented in the supplementary data. The following electronic databases were searched from inception to April 2021: MEDLINE, EMBASE, CINAHL, Scopus, Web of

Science, Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), and the Cochrane Methodology Register), the Allied and Complementary Medicine Database (AMED), PROSPERO, and the NIHR Centre for Reviews and Dissemination database. Finally, we hand-searched reference lists of included papers to identify any additional studies for inclusion. Following the removal of duplicates, titles and abstracts, all articles identified from the searches were independently screened by two review authors (R. A. W. and T. F.) to identify articles potentially eligible for inclusion. Both review authors then independently evaluated full articles against the inclusion and exclusion criteria. Any disputes during the screening process were resolved through discussion between the two review authors, or with the wider review team when necessary.

2.4 | Data extraction

Data extraction was performed independently by two review authors (RAW and LC) using a standardised data extraction form. The following information was extracted from each article: study characteristics (lead author, date of publication), design, duration of follow-up, setting, country, sample size, population (type and severity of condition), mean age and age range, treatment regimen, intervention, comparator, outcome measures, and summary of findings. Any inconsistencies during the data extraction process were investigated and discussed by both review authors, and resolved through discussion with a third review author (HJS) when necessary.

2.5 | Assessment of methodological quality

Two review authors (RAW, LC) independently assessed risk of bias for each included study using the Joanna Briggs Institute Critical Appraisal checklist for quasi-experimental non-randomised studies.[33] No study was excluded from analysis on the basis of methodological quality. Assessment findings were presented narratively and in a table displaying the frequency of each classification.

2.6 | Analysis

Following the assessment of methodological quality, data were synthesised according to outcome variables. The included studies were too heterogeneous with regards to participants, interventions, and outcomes to warrant statistical pooling of data, therefore a narrative analysis was undertaken.

3 | RESULTS

3.1 | Study selection

The search yielded 165 records, of which 35 were retrieved for full-text screening. Ten studies met our inclusion criteria. The full selection process is illustrated in a PRISMA 2020 flow diagram (Figure 1).

3.2 | Quality assessment of included studies

Results of the methodological quality assessment are presented in Table 1. All ten studies provided a clear description of cause and effect. Participants received similar treatment and care in three studies[34–36]; this was unclear in the remaining seven studies. In four studies, it was unclear if participant demographics were similar due to the type of haemophilia, severity of haemophilia or age range not being reported[37–40] and in a fifth study participants were not similar (some had arthropathy in joints other than the ankle whereas others did not).[27] Only two studies included an independent control or comparison group.[27,38] In six studies, there were multiple measurements of the outcome both before and after the intervention,[27,34,38,40–42] and seven studies either completed follow-up or described incomplete follow-up.[27,34,38–42] Three laboratory-based studies tested participants during a single session, therefore multiple measurements and assessment of follow-up were not applicable.[37,43,44] Outcomes of participants included in comparisons were measured in the same way in nine of the ten studies,[27,34,37–39,41–44] and the outcome measures selected were reliable in eight studies.[27,34,37,39,41–44] In one study, it was unclear how bleeding rates was measured,[40] while another study used the American Orthopaedic Foot & Ankle Society (AOFAS) Ankle–Hindfoot scale,[38] which lacks evidence for reliability, content validity, responsiveness and measurement error.[45] Eight of the ten studies reported probability values and were considered to have used appropriate statistical tests[27,34,38–40,42–44]; one study reported probability values and used appropriate statistical tests for one outcome but not others,[41] and one study did not carry out any statistical analyses.[37]

3.3 | Characteristics of included studies

An overview of study characteristics is presented in Table 2. All studies were non-randomised and three employed a within-subject study design.[37,43,44] The within-subject studies had no further follow-up[37,43,44]; the duration of further follow-up in the remaining seven studies ranged from 6 weeks to 12 months.[40,41] Participants were recruited from eight different countries: UK, USA, Spain, Brazil, Belgium, Australia, Japan, and Germany.[27,34,37–44] The number of participants per study ranged from 9 to 94[38,43] with a total number of participants across all studies being 271.[27,34,37–44] All participants had haemophilia; 135 had haemophilia A, 13 had haemophilia B, and the type of haemophilia was unspecified for the remaining 123 participants.[27,34,37–44] One hundred and sixteen participants had severe haemophilia, 22 participants had moderate haemophilia and 13 had mild haemophilia. Severity of haemophilia was not specified for 120 participants. Three studies did not report the age range of participants.[37,38,40] In the remaining seven studies, participant age ranged from three to 70 years. Forty-four participants were on prophylaxis treatment, whilst 19 participants were taking treatment on-demand. Treatment types were not specified for the remaining participants.

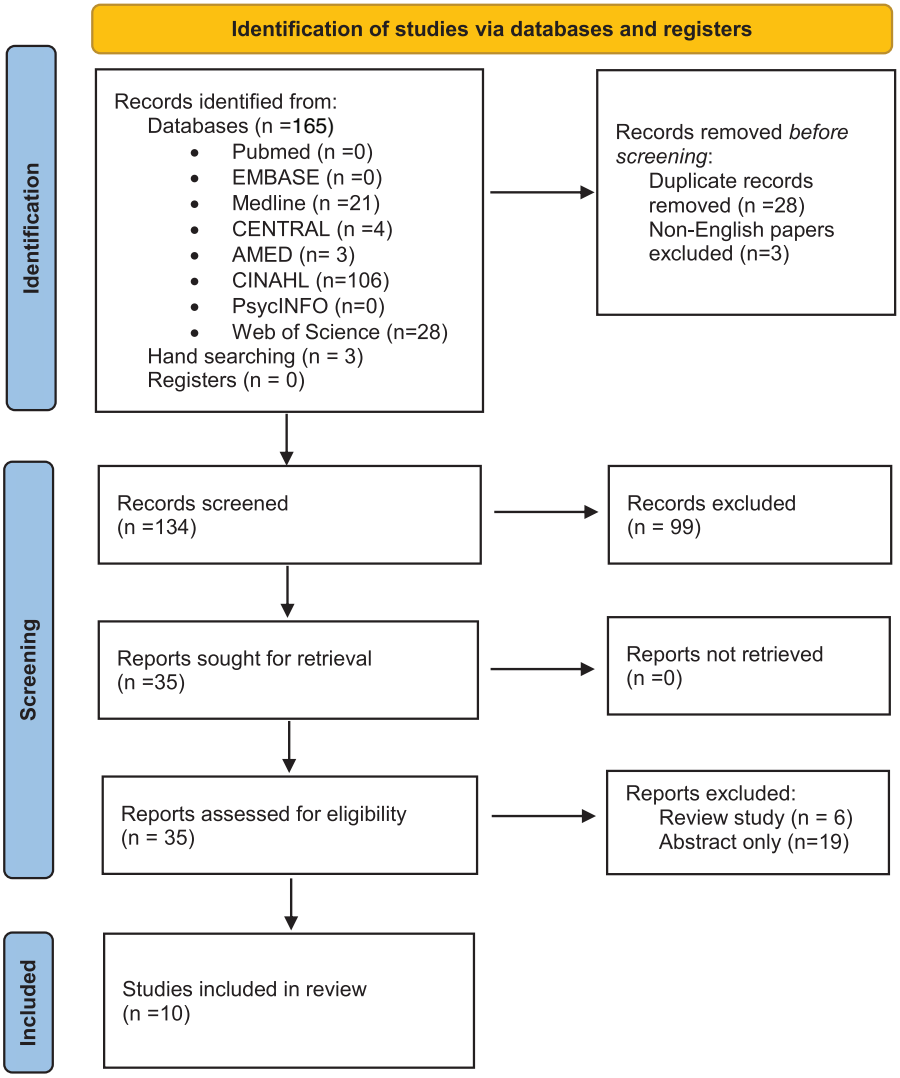

FIGURE 1 PRISMA 2020 flow chart showing literature search process

3.4 | Interventions

A range of interventions were evaluated. Four studies were single-arm with no comparator, exploring the following interventions: Airstirrup ankle splint[39]; FO[40,41]; and a multidisciplinary physiotherapy-podiatry service which included FO provision.[34] Three studies compared one intervention against another intervention(s): shoes versus FO[27]; different footwear types[43]; various ankle supports (AFO, FO, shoe modifications, elastic ankle supports).[42] Two studies compared an intervention(s) against no intervention: FO[38]; silicone heel cushion.[37] One study compared two interventions (AFO, fracture boot) against each other and against no intervention.[44]

3.5 | Bleeding incidence

Four studies measured the incidence of bleeding following intervention with footwear and/or orthotic devices.[34,39,41,42] The use of an Airstirrup splint resulted in a clinically meaningful reduction in the incidence of ankle joint bleeding when compared to episodes before the intervention; this was most effective in children between the ages of 3 and 9 years.[39] A significant reduction in the frequency of ankle joint and rearfoot bleeding incidence was observed following the use of FO,[41] and also following the use of elastic ankle supports.[42] Shoe modifications and AFO also reduced the number of ankle joint bleeding episodes, but not significantly,[42] and a multidisciplinary combined physiotherapy-podiatry clinic, which included the provision of FO, did not result in a statistically significant difference in the number of ankle joint bleeding episodes.[34] A fifth study also reported a reduction in ankle joint bleeding episodes following the use of FO, but no statistical analysis was performed.[40] However, one study reported an increase in the incidence of traumatic bleeding following FO use.[41]

3.6 | Clinical assessment

3.6.1 | Ankle joint range of motion (ROM)

Ankle joint ROM was an outcome measure in three studies,[37,39,42] with alignment measured as part of the AOFAS Ankle–Hindfoot Scale in a

TABLE 1 Summary of methodological quality assessment

Study ID	Is it clear in the study what is the 'cause' and what is the 'effect'	Were the participants included in any comparisons similar?	Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Was there a control (or comparison) group?	Were there multiple measurements of the outcome both pre and post the intervention/ exposure?	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Was appropriate statistical analysis used?
Buzzard 2009[39]	Yes	Unclear	Unclear	No	No	Yes	Yes	Yes	Yes
De la Corte-Rodriguez 2019[38]	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	No	Yes
Dodd 2020[34]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Jorge Filho 2006[41]	Yes	Yes	Unclear	No	Yes	Yes	Yes	Yes	Yes for bleeding episodes but not for gait measures
Lobet 2012[27]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
McLaughlin 2013[43]	Yes	Yes	Unclear	No	N/A	N/A	Yes	Yes	Yes
Oleson 2017[44]	Yes	Yes	Unclear	No	N/A	N/A	Yes	Yes	Yes
Seuser 1997[37]	Yes	Unclear	Unclear	No	N/A	N/A	Yes	Yes	N/A
Slattery 2001[40]	Yes	Unclear	Unclear	No	Yes	Yes	Unclear (bleed rate)Yes - FFI	Unclear (bleed rate)Yes – FFI	Yes
Tanaka 1996[42]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes

Abbreviation: FFI, Foot Function Index.

TABLE 2 Summary of studies included in review

Study ID	Study design	Duration of follow-up	Setting (country)	Sample size	Population	Mean age (SD); age range	Treatment regimen	Intervention	Comparator	Outcome measures	Adverse events	Key findings
Buzzard 2009[39]	Quasi-experimental	6 months	Hospital (UK)	19	Haemophilia A or B and history of ankle haemarthrosis – breakdown of sample not reported; all severe	Mean age 6.6 (SD not reported); age range 3–17	Not reported	Airstrrup ankle splint	N/A	Number of bleeding episodes Ankle ROM (measured with a goniometer); muscle power using the Oxford Scale; muscle bulk; proprioception	Pressure sore ($n = 1$)	Significant reduction in the number of haemorrhages following use of the splint, most effective in children between the ages of 3 and 9 years. No decrease in any joint ROM, no decrease in muscle bulk, and no decrease in muscle power. There was an increase in proprioception in all children. The effect of the intervention was significant ($p = .020$). There were significant differences between the number of haemorrhages pre-, during and post-intervention. Throughout the 6-month post-trial period 17 of the 19 children began to bleed again into the target joint, but not to the same extent as pre-trial. Statistical analysis showed that the ankle splint ad some long-lasting effect for the right ($p = .189$) and for the left ($p = .130$).
De la Corte-Rodriguez 2019[38]	Quasi-experimental	6 months	Hospital (Spain)	94	Not reported	Mean age 37.8 (SD 14.3); age range not reported	Not reported	FO (prescription individualised, e.g., 2–5 mm medial or lateral wedge from centre of heel to talonavicular joint, MLA arch support, heel raise, metatarsal bar with heel cushioning)	No orthoses	Pain, function and alignment - AOFAS Ankle-Hindfoot Scale	No adverse events reported	Significant improvement on AOFAS Ankle-Hindfoot scale for orthoses group ($p < .001$) - improvement obtained with respect to pain and function but not alignment. No significant changes in AOFAS Ankle-Hindfoot Scale amongst no orthoses group ($p < .276$).

(Continues)

TABLE 2 (Continued)

Study ID	Study design	Duration of follow-up	Setting (country)	Sample size	Population	Mean age (SD); age range	Treatment regimen	Intervention	Comparator	Outcome measures	Adverse events	Key findings
Dodd 2020[34]	Quasi-experimental	6 months	Hospital (UK)	27 (two lost to follow up)	25 with haemophilia A, two with haemophilia B; 17 severe, three moderate, seven mild.	Mean age 23.9; Range 4–70.	Prophylaxis ($n = 17$); on-demand ($n = 10$)	Multidisciplinary podiatry-physiotherapy clinic including provision of FO (including prefabricated and custom FO made to particular specifications, including rearfoot and forefoot posting, and heel raises).	N/A	Ankle AJBR; satisfaction questionnaire; HJHS	No adverse events reported	No statistically significant difference in post-intervention ankle AJBR when compared to pre-intervention ($p = .158$). All participants who completed the satisfaction questionnaire ($n = 16$) agreed or strongly agreed that they were satisfied with the new clinic. No statistically significant difference in the post-intervention ankle joint HJHS when compared to the pre-intervention score ($p = .904$).
Jorge Filho 2006[41]	Quasi-experimental	6 months	Rehabilitation centre (Brazil)	43	39 with haemophilia A, four with haemophilia B; 22 severe, 15 moderate, six mild	Mean age 16.1 (SD not reported) age range 5–58	Not reported	FO (prescription individualised – some with metatarsal dome, lateral or medial rearfoot wedge, some Air Stirrup orthoses in addition).	N/A	Number of bleeding episodes; rearfoot and ankle joint stability – COP trajectory using F-scan	Increase in the number of traumatic ankle bleeds.	Significant reduction in the frequency of spontaneous bleeding events ($p < .001$). Increase in the number of traumatic ankle bleeds ($p = .004$). FO controlled the instability of the rear foot. Full plantar pressure data not reported
Lobet 2012[27]	Quasi-experimental	40 weeks (+/- 18 weeks)	Hospital (Belgium)	16	15 with haemophilia A, one with haemophilia B; 13 severe, three moderate	Mean age 41 (SD 11); age range 21–60	Prophylaxis ($n = 7$); on-demand (n-9)	Casted FO (high-density polyethylene foam or leather-lined cork, with extra-density padding proximal to the metatarsals).	Orthopaedic shoes with insoles (podofoam)	FFI-R short-form; patient satisfaction questionnaire; 3D gait analysis (spatiotemporal parameters, kinematics and kinetics – using an instrumented treadmill); mechanics and metabolic measurements	Two participants abandoned the orthoses because of increased ankle pain due to Achilles tendonitis (diagnosed by clinical examination).	63% of participants were satisfied with the FO/orthopaedic footwear. Total FFI-R score significantly decreased in participants who reported being satisfied ($p = .007$), attributed to a reduction in the FFI pain subscale. No significant change was observed in those being non-satisfied. FO had a significant effect of foot progression angle (external foot rotation) of 3.1° when using an FO (19.7° vs. 16.6°, $p < .001$)

(Continues)

TABLE 2 (Continued)

Study ID	Study design	Duration of follow-up	Setting (country)	Sample size	Population	Mean age (SD); age range	Treatment regimen	Intervention	Comparator	Outcome measures	Adverse events	Key findings
												FO had limited impact on gait pattern (no impact on ankle kinetics or kinematics). Orthopaedic footwear had a significant influence on spatiotemporal parameters, kinematics and kinetics (decrease in cadence of 4.5 step per minute, $p < .001$), increase in step length, $p = .012$, increase in total hip and knee ROM in swing phase increased by 3.1 degrees ($p = .011$) and 4.4 degrees ($p < .001$), respectively, increase in peak ankle plantarflexion moment by 30 N m kg^{-1} ($p < .001$). Biomechanical changes induced by the shoes and FO were independent of their ability to improve comfort, while being insufficient to influence knee and hip kinematics and kinetics, or mechanical and energetic variables. Overall, the mechanical and energetic variables were not influenced by the FO or orthopaedic footwear, except for the 'recovery' index, which was significantly increased by 2.2% ($p = .037$).

(Continues)

TABLE 2 (Continued)

Study ID	Study design	Duration of follow-up	Setting (country)	Sample size	Population	Mean age (SD); age range	Treatment regimen	Intervention	Comparator	Outcome measures	Adverse events	Key findings
McLaughlin 2013[43]	Within-subject experimental	N/A	Hospital (UK)	9	seven with haemophilia A, two with haemophilia B; all severe.	Mean age and SD not reported; age range 28–49	Not reported	Neutral cushioned sports trainer	Conventional footwear	Ankle kinematic and kinetic data (using Coda motion analysis and a force plate, and 2D modelling software); kinematic and kinetic variables of the hip and knee	No adverse events reported	Increase in intra-articular force in the ankle when wearing the trainer compared to conventional footwear; increase in ankle joint force on both the right and left ankle when wearing the trainer compared to conventional footwear. Left ankle force increased by 12.4%, 1.37 → 1.54 BW ($p = <.01$) whilst in the trainer, the right ankle force increased by 15.6%, 1.41 → 1.63 BW ($p < .0001$). Hip and knee variables not reported in the results.

(Continues)

TABLE 2 (Continued)

Study ID	Study design	Duration of follow-up	Setting (country)	Sample size	Population	Mean age (SD); age range	Treatment regimen	Intervention	Comparator	Outcome measures	Adverse events	Key findings
Oleson 2017[44]	Within-subject experimental	N/A	Haemophilia centre (USA)	17	14 haemophilia A, three haemophilia B; all severe.	Mean age and SD not reported; age range 15–48	Not reported	Carbon fibre floor reaction AFO	Fracture boot No brace (shoes only)	Pain (11-point NPRS) Temporal and spatial gait parameters (Gaitrite)	No adverse events reported	Pain is reduced significantly ($P < 0.05$) with both brace models compared with shoes only (no brace) condition. There is no difference in pain reduction between FB and carbon fibre AFO treatments ($P = 0.999$). Pain significantly reduced with both brace models ($p < 0.05$) compared with no brace. There was difference between fracture boot and AFO treatments. Use of fracture boot altered gait parameters that are associated with movement of the affected and the unaffected limb during the gait cycle, whereas the use of the AFO did not affect the gait cycle. The following treatment effects were noted: 1. Cadence is decreased compared to either the no brace or CF-AFO condition. 2. Step time, cycle time and swing time demonstrate significant increase at the $P < 0.05$ value on both involved and uninvolved limbs compared to the non-braced condition. 3. Cycle time showed significant increase on the involved limb when compared to the CF-AFO. 4. Stance time shows a significant increase in the uninvolved limb compared to the other two conditions. 5. There is no difference in any gait parameter when the carbon fibre AFO is compared to the no brace condition

(Continues)

TABLE 2 (Continued)

Study ID	Study design	Duration of follow-up	Setting (country)	Sample size	Population	Mean age (SD); age range	Treatment regimen	Intervention	Comparator	Outcome measures	Adverse events	Key findings
Seuser 1997[37]	Within-subject experimental	N/A	Haemophilia centre (Germany and UK)	10	Not reported	Not reported	Not reported	Silicone heel cushion (Viscoheel) in trainer	No heel cushion	Ankle and STJ ROM, using a goniometer; maximum angular velocity and acceleration at ankle and STJ, using online motion analysis/ultrasound topmeter)	No adverse events reported	Participants with less haemarthropathy had a change in gait pattern using silicone heel cushion. Influence of heel cushion diminished with restricted ankle motion. In six participants, velocity and acceleration increased with silicone heel cushion and increased ROM. In four participants, gait data was not reported. Silicone heel cushioning had no influence on ankles in the late stage of haemarthropathy. No statistical analysis carried out.
Slattery 2001[40]	Quasi-experimental	6 weeks	Haemophilia Association (Australia)	16	All haemophilia A; severity not reported	24 (SD 6.2); age range not reported	Not reported	Casted FO (4 mm polypropene Root orthoses with a 4 degree rearfoot post)	N/A	Number of bleeding episodes; FFI	No adverse events reported	Reduction in ankle bleeds (patient-reported - no statistical analysis). Significant reduction in level of pain under orthoses (FFI pain subscale – $p < .05$). No significant improvement in difficulty or activity. Overall FFI significant improvement after the use of orthoses ($p < .05$).
Tanaka 1996[42]	Quasi-experimental	12 months	Haemophilia centre (Japan)	20	19 with haemophilia A, one with haemophilia B; 19 severe, one moderate.	Mean age 17.6 (SD 10.4); age range 6–41	Prophylactic therapy ($n = 20$)	Ankle support (including AFOs, FO, shoe modifications and elastic ankle supports)	N/A	Number of bleeding episodes; ROM of shoulders, elbows, hips, knees, and ankles, using a goniometer; X-rays.	In one participant, a plastic AFO increased bleeds	Significant decrease of haemorrhaging in the ankle joint with the elastic supporter ($p < .05$). Orthotic management reduced haemorrhaging frequency compared with the frequency before the treatment – only significant with elastic supporter. Ankle ROM after the orthotic management increased, but not significantly. X-rays – no significant change.

Abbreviations: AFO, ankle-foot orthosis; AJBR, annualised joint bleed rate; AOFAS, American Orthopaedic Foot and Ankle Society; BW, body weight; CoP, centre of pressure; FFI, Foot Function Index; FFI-R, Foot Function Index-Revised; FO, foot orthoses; HJHS, Haemophilia Joint Health Score; MLA, medial longitudinal arch; NPRS, numerical pain rating scale; ROM, range of motion; SD, standard deviation; STJ, subtalar joint.

fourth.[38] One of these studies also included subtalar ROM as an outcome measure,[37] and another included ROM of the shoulder, elbow, hip and knee joints.[42] There was no change in ankle joint ROM following the use of the Airstirrup ankle splint.[39] In one study, the authors reported an increase in ankle joint ROM with the use of orthotic devices (including AFO, FO, shoe modifications and elastic ankle support); however, these changes were not significant.[42] Another study indicated that ankle joint ROM increased following the use of a silicone heel cushion, but no statistical analysis was performed.[37] There was no significant improvement in ankle joint alignment on the AOFAS Ankle–Hindfoot scale following the use of FO.[38]

3.6.2 | Haemophilia Joint Health Score (HJHS)

One study utilised the HJHS and found no significant difference in ankle joint HJHS scores following a multidisciplinary combined physiotherapy-podiatry clinic intervention that included the provision of FO.[34]

3.7 | Patient-reported outcomes

3.7.1 | Pain

Four studies measured patient-reported pain.[27,38,40,44] FO significantly reduced pain on the AOFAS Ankle–Hindfoot Scale,[38] whilst AFOs and fracture boots both significantly reduced pain on a numerical pain rating scale.[44] Orthopaedic shoes and FO significantly reduced pain on the Foot Function Index-Revised (FFI-R) pain subscale.[27] Similarly, FO significantly reduced pain on the FFI pain subscale.[40]

3.7.2 | Function

Three studies measured function.[27,38,40] A significant improvement in overall function on the FFI was reported with the use of FO.[40] However, this improvement was obtained with respect to pain only; there was no significant improvement in difficulty or activity subscales of the FFI. Similarly, a significant improvement in overall function on the FFI-R occurred after the use of both FO and orthopaedic shoes amongst satisfied participants, but only the improvement with regards to the pain subscale was statistically significant.[27] However, in another study, FO significantly improved function on the AOFAS-AH scale.[38]

3.7.3 | Patient satisfaction

Two studies measured patient satisfaction using bespoke[34] or modified self-reported satisfaction questionnaires.[27] In one study, 63% of participants reported satisfaction with footwear and orthotic devices.[27] In the other study, 100% of participants either agreed or strongly agreed that they were satisfied with a multidisciplinary combined physiotherapy-podiatry clinic which included FO provision; however, questionnaire completion rate was 57.1%.

3.8 | Biomechanical outcome measures

3.8.1 | Temporal and spatial parameters

Two studies measured temporal and spatial parameters.[27,44] In the one study, FO had no influence on gait variables except significantly decreased cadence amongst participants who reported satisfaction with the FO, whereas orthopaedic shoes significantly increased step length and decreased cadence, regardless of satisfaction.[27] In the second study, use of a fracture boot significantly reduced cadence compared to use of an AFO and compared to no intervention, significantly increased step time, cycle time, and swing time when compared to no intervention, and significantly increased gait cycle time compared to use of an AFO.[44] No difference in gait variables was found between use of an AFO and no intervention.[44]

3.8.2 | Lower limb kinetics and kinematics

Three studies investigated kinetics and kinematics.[27,37,43] One study found that orthopaedic shoes with FO had a significant influence on ankle joint kinematics and kinetics, whilst FO significantly reduced foot progression angle (external foot rotation) when compared to no FO.[27] Orthopaedic shoes were shown to significantly improve the propulsive function of the ankle, by increasing the peak ankle plantarflexion moment. Neither FO nor orthopaedic shoes impacted metabolic cost, mechanical work or gait efficiency.[27] Another study demonstrated increased peak ankle joint force during midstance when participants wore a neutral-cushioned sports trainer compared to a conventional shoe.[43] In a third study, ankle and subtalar joint velocity and acceleration increased with the use of a silicone heel cushion in early haemarthropathy but did not influence the later stages of the condition when ROM was reduced; however, no statistical analysis was carried out in this study.[37] In terms of hip and knee kinematics, only orthopaedic shoes were reported to have a significant impact.[27] One study reported that FO improved centre of pressure trajectory, leading to improved rearfoot and ankle joint stability although again, no statistical analysis of biomechanical data was conducted.[41]

3.9 | Adverse effects

Four studies reported adverse effects, all of which were minimal. In one study, two participants reported increased ankle pain following the use of footwear/orthotic devices.[27] In another study, the Airstirrup splint caused a pressure ulcer in one participant.[39] Two participants wearing FO provided as part of a multidisciplinary podiatry-physiotherapy clinic had activity-related bleeds, whilst one participant developed chronic synovitis in the ankle and two others had an increase

in loss of ROM.[34] In the fourth study reporting adverse effects, one participant had an increase in bleeding episodes following the use of a plastic AFO.[42]

4 | DISCUSSION

This systematic review aimed to summarise and synthesise evidence relating to the efficacy and effectiveness of footwear and orthotic devices in the management of ankle joint haemarthrosis and haemarthropathy in adults and children with haemophilia. There were several methodological limitations to the studies included in this review; there was no randomisation or blinding in any of the studies, and only two studies included a concurrent comparison or control group. Additionally, sample sizes in most of the studies were small and follow-up was limited. Several inconsistencies were encountered when reviewing the studies, making it difficult to generalise the findings, including the type of device used and different outcome measures utilised. Our review findings should therefore be interpreted with caution.

These findings indicate that the use of footwear and orthotic devices may have the potential to reduce ankle joint bleeding episodes in haemophilia, highlighting their potential in providing clinical benefit following acute haemarthrosis and during periods of rehabilitation. However, a shift in treatment regimens for people with haemophilia over the last decade, with higher trough levels, extended half-life products and emerging novel bispecific monoclonal antibodies, has already led to a significant reduction in the incidence of haemarthrosis. Whilst each episode of bleeding can contribute to long term irreversible joint damage, measurement of ankle joint bleeding rate may become difficult to identify clinically in developed healthcare systems.[46]

Our findings also suggest that in a broad range of outcome measures footwear and orthotic devices can alter foot and ankle joint kinetics and kinematics in the presence of haemarthropathy. This is consistent with existing clinical trials investigating FO and footwear interventions for foot and ankle pathologies in IA and OA.[16,47] Further research is needed to explore the biomechanical outcomes of orthotic devices and footwear in ankle joint haemarthrosis and haemarthropathy, and to ascertain the mechanism by which footwear and orthotic devices exert their action.

The appropriateness of FO is an important factor to consider in the clinical management of ankle haemarthrosis and haemarthropathy. Softer, cushioning orthoses may improve comfort at weight-bearing areas caused by hindfoot and plantarflexion deformities,[48] Supporting splints and AFO often limit ROM by partial or full ankle joint immobilisation[22,39] although none of the studies in our review specifically measured comfort. Rigid carbon fibre orthoses have been shown to prevent foot deformities and improve pain and function in other conditions.[47] Our review indicated that the use of FO has the potential to prevent or correct biomechanical changes associated early and moderate ankle haemarthropathy where ankle ROM becomes impeded and pain becomes a driver of decline,[49] but further research is required to determine what type of FO is most appropriate.

Haemarthrosis is associated with the decline in joint structure and function that becomes a source of pain as joint health declines.[35,50] In agreement with previous literature in other arthropathies,[51,52] our findings suggest a potential to reduce patient-reported pain with the use of footwear and orthotic devices has been shown to affect treatment compliance.[53] Although the clinical benefits of specialist footwear are evident across a range of foot disorders, patient dissatisfaction concerning aesthetics, perceived comfort and poor fit are consistently reported, leading to reduced or non-usage.[54,55] Our review suggested adequate patient satisfaction with footwear and orthotic devices for ankle joint pathology in haemophilia, but this outcome was explored in only two of the ten studies. A core set of outcomes for studies involving people with haemarthropathy, developed with patients, clinicians and researchers, is needed to ensure future study findings are relevant and transferable to clinical practice.

4.1 | Strengths and limitations

To our knowledge, this is the first systematic review evaluating footwear and orthotic devices in the management of ankle haemarthrosis and haemarthropathy in haemophilia. We undertook extensive searches with no restrictions on study type to identify all studies published to date on this topic, and the risk of bias was critically assessed by two reviewers independently. We acknowledge, however, that by restricting studies to the English language, potentially relevant papers may have been excluded. Notably, the majority of studies included in our review were conducted in high-income countries where advanced factor and non-factor treatments are more widely accessible. Therefore, our findings may not be generalisable to the global haemophilia population. Additionally, limited details were provided on participants' pharmacological treatment or changes to pharmacological treatment regimens during the study periods. Changes in pharmacological management such as an increase in factor dose over the course of a study could affect outcomes such as annual joint bleed rate, thus confounding true orthotic device and footwear effects. Future research must account for the inclusion of haemostatic variables as a primary study characteristic.

5 | CONCLUSION

Ankle joint haemarthrosis and resultant haemarthropathy in people with haemophilia are associated with significant pain and disability. This systematic review has identified a lack of high-quality evidence regarding the efficacy and effectiveness of footwear and orthotic devices in the management of this condition. Limited findings from non-randomised studies suggest that footwear and orthotic devices have some potential to reduce the incidence of ankle haemarthrosis, improve ankle joint kinetics and kinematics, and improve patient-reported pain. Future randomised trials with adequate sample sizes, long term follow-up, and standardised, validated outcome measures, are urgently needed to inform the management of ankle joint

haemarthrosis and haemarthropathy in haemophilia and underpin clinical practice.

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CONFLICT OF INTEREST

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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