

Osteoarthritis and Cartilage



Review

International Foot and Ankle Osteoarthritis Consortium review and research agenda for diagnosis, epidemiology, burden, outcome assessment and treatment



International Foot and Ankle Osteoarthritis Consortium, J.B. Arnold [†], C.J. Bowen ^{‡§}, L.S. Chapman ^{||}, L.S. Gates ^{‡§}, Y.M. Golightly [¶], J. Halstead ^{||#}, M.T. Hannan ^{††}, H.B. Menz ^{‡‡§§*}, S.E. Munteanu ^{‡‡}, K.L. Paterson ^{|||}, E. Roddy ^{§§¶¶}, H.J. Siddle ^{||}, M.J. Thomas ^{§§¶¶}

[†] IIMPACT in Health, Allied Health and Human Performance, University of South Australia, Adelaide, South Australia, 5000, Australia

[‡] School of Health Sciences, University of Southampton, Building 67, University Road, Southampton, SO17 1BJ, UK

[§] Centre for Sport, Exercise and Osteoarthritis Research Versus Arthritis, University of Southampton, Southampton, SO17 1BJ, UK

^{||} Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, LS2 9JT, UK

[¶] Department of Epidemiology, Gillings School of Global Public Health, Thurston Arthritis Research Center, University of North Carolina at Chapel Hill, 3330 Thurston Building, CB 7280, Chapel Hill, NC 27599, USA

[#] Podiatry Services, Leeds Community Healthcare NHS Trust, Leeds, LS6 1PF, UK

^{††} Hinda and Arthur Marcus Institute for Aging Research, Hebrew SeniorLife, Beth Israel Deaconess Medical Center, And Harvard Medical School, Boston, MA, 02108, USA

^{‡‡} School of Allied Health, Human Services and Sport, La Trobe University, Melbourne, Victoria, 3086, Australia

^{§§} Primary Care Centre Versus Arthritis, School of Medicine, Keele University, Keele, Staffordshire, ST5 5BG, UK

^{|||} Centre for Health, Exercise and Sports Medicine, School of Health Sciences, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Melbourne, Victoria, 3010, Australia

^{¶¶} Haywood Academic Rheumatology Centre, Midlands Partnership NHS Foundation Trust, Haywood Hospital, Burslem, Staffordshire, ST6 7AG, UK

ARTICLE INFO

Article history:

Received 25 November 2021

Accepted 3 February 2022

Keywords:

Osteoarthritis

Foot

Consensus

Review

SUMMARY

Objective: To summarise the available evidence relating to the diagnosis, epidemiology, burden, outcome assessment and treatment of foot and ankle osteoarthritis (OA) and to develop an agenda to guide future research.

Method: Members of the International Foot and Ankle Osteoarthritis Consortium compiled a narrative summary of the literature which formed the basis of an interactive discussion at the Osteoarthritis Research Society International World Congress in 2021, during which a list of 24 research agenda items were generated. Following the meeting, delegates were asked to rank the research agenda items on a 0 to 100 visual analogue rating scale (0 = not at all important to 100 = extremely important). Items scoring a mean of 70 or above were selected for inclusion.

Results: Of the 45 delegates who attended the meeting, 31 contributed to the agenda item scoring. Nineteen research agenda items met the required threshold: three related to diagnosis, four to epidemiology, four to burden, three to outcome assessment and five to treatment.

Conclusions: Key knowledge gaps related to foot and ankle OA were identified, and a comprehensive agenda to guide future research planning was developed. Implementation of this agenda will assist in improving the understanding and clinical management of this common and disabling, yet relatively overlooked condition.

© 2022 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.

Background

Foot and ankle osteoarthritis (OA) is common and disabling but has received less research attention than OA at other sites^{1,2}. To

* Address correspondence and reprint requests to: H.B. Menz, School of Allied Health, Human Services and Sport, La Trobe University, Melbourne, Victoria 3086, Australia.

E-mail address: h.menz@latrobe.edu.au (H.B. Menz).

address this, an international group of expert foot and ankle clinicians and researchers was formulated in 2018 and the resulting International Foot and Ankle Osteoarthritis Consortium (IFOAC) was launched at the Osteoarthritis Research Society International (OARSI) 2019 World Congress. In 2020/2021, the consortium steering group decided to develop a preliminary research agenda based on an assessment of evidence gaps and the views of clinicians and researchers working in the field of foot and ankle OA. In this paper, we present the narrative literature review underpinning this activity and report the results of a research agenda meeting conducted at the OARSI 2021 World Congress.

Methods

During 2020/2021, the consortium steering group compiled a document summarising the evidence concerning the diagnosis, epidemiology, burden, outcome assessment and treatment of foot and ankle OA, and based on an evaluation of evidence gaps, proposed a list of future research agenda items. In developing the document, we relied on recent systematic^{3–6} and narrative reviews^{1,7–11} and the combined knowledge and expertise of the consortium members, all of whom have published extensively in the field of foot and ankle OA. The document was then circulated to a panel of 45 delegates who had registered for the IFOAC discussion group meeting at the OARSI World Congress held on May 6, 2021. During the meeting, the group divided into five breakout rooms where evidence relating to diagnosis, epidemiology, burden, outcome assessment and treatment was discussed, and research agenda items were further developed. Following the meeting, we used an online survey platform (QuestionPro, Austin TX, USA) to invite delegates by email to rank the research agenda items on a 0–100 visual analogue rating scale (0 = not at all important, 100 = extremely important). We used an arbitrary mean threshold of ≥ 70 to identify items considered to be the most important.

Results

Thirty-one (69%) delegates from seven countries responded to the online survey. Characteristics of the respondents are provided in Table I. Mean (SD) scores for each research agenda item are shown in Table II. In the following section, we present the results of the narrative review and report the corresponding research agenda items that met the ≥ 70 ranking threshold.

Definition and diagnosis

Imaging diagnosis

Traditionally, radiographic diagnosis of OA adopts the Kellgren and Lawrence (KL) system¹². However, this system was developed for knee OA^{13,14} and may not be valid for the foot and ankle. The La Trobe Foot Atlas was developed to diagnose radiographic OA (rOA) of the first metatarsophalangeal (MTP) joint, first cuneiform-metatarsal joint, second cuneiform-metatarsal joint, talonavicular joint, and navicular-first cuneiform joint¹⁵. The atlas uses dorso-plantar and lateral radiographic projections, and grades the presence of osteophytes and joint space narrowing (JSN) separately on a scale from 0 (absent) to 3 (severe osteophyte or joint fusion). The overall score has demonstrated moderate-to-excellent reliability¹⁵.

Ankle joint images have recently been incorporated into the La Trobe Foot Atlas⁶, and a separate bespoke atlas has been developed for the ankle and rearfoot¹⁶. Like the La Trobe Foot Atlas, the ankle/rearfoot atlas grades osteophytes and JSN on a 0 to 3 scale using mortise and lateral projections for the tibiotalar, talofibular and subtalar joints. Intra-rater reliability for most features was good-to-

Age, years – mean (SD), range	44.9 (11.2), 27 – 74
Sex – n (%)	
Female	18 (58.1)
Male	13 (41.9)
Country of residence – n (%)	
United Kingdom	11 (35.5)
Australia	10 (32.3)
United States	5 (16.1)
The Netherlands	2 (6.5)
Canada	1 (3.2)
Spain	1 (3.2)
Hungary	1 (3.2)
Academic/professional background – n (%)	
Podiatrist	13 (41.9)
Physiotherapist/physical therapist	6 (19.4)
Rheumatologist	2 (6.5)
Biomechanist	2 (6.5)
Athletic trainer	2 (6.5)
Epidemiologist	2 (6.5)
Medical engineer	1 (3.2)
General practitioner	1 (3.2)
Physiatrist	1 (3.2)
Current role – n (%)	
Combination of research and clinical practice	13 (41.9)
Full-time research	12 (38.7)
University academic/lecturer	6 (19.4)
Attended OARSI discussion group – n (%)	27 (87.1)

Table I

Osteoarthritis and Cartilage

Characteristics of delegates who completed the scoring of research agenda items ($n = 31$)

excellent, whereas inter-rater reliability ranged from fair-to-excellent.

Magnetic resonance imaging (MRI) scoring systems to assess the whole joint complex are emerging for the foot and ankle. A semi-quantitative MRI scoring system for the first MTP joint demonstrated excellent intra-rater and inter-rater reproducibility^{17,18}. A recent subtalar and talonavicular joint scoring system reported excellent overall intra-rater and inter-rater correlation¹⁹. Preliminary examination across the hindfoot, midfoot and MTP joints demonstrated good intra-rater reliability and fair inter-rater reliability when features across subregions are scored collectively²⁰. A proposed ankle OA MRI scoring system demonstrated 'substantial' to 'almost perfect' intra-rater and inter-rater reproducibility²¹.

Other imaging modalities may provide additional benefits. Ultrasound is a reliable tool for assessing synovial hypertrophy, joint effusion, and power Doppler signal, but further studies are required to determine its potential in assessing cartilage damage and osteophytes²². A formal weight-bearing computerised tomography foot/ankle OA scoring system has yet to be developed²³.

Clinical diagnosis

Clinical definitions for OA at the knee²⁴, hip²⁵ and hand²⁶ have existed for decades, but no definition exists for foot or ankle OA. Observed radiographic OA and pain in the corresponding area has defined symptomatic radiographic foot OA (srOA)²⁷. It is unclear whether a stand-alone clinical definition is necessary or possible, however an agreed definition could reduce reliance on imaging. Whether separate clinical definitions for different foot and ankle regions are necessary remains unclear²⁸.

	Item	Mean (SD)
Diagnosis	1. Develop an overarching clinical definition of foot and ankle OA	82.6 (21.3)
	2. Develop clinical diagnostic criteria for midfoot and ankle OA	85.9 (10.4)
	3. Evaluate first MTPJ OA diagnostic criteria in a larger cohort and a range of forefoot conditions	66.4 (22.7)
	4. Develop foot OA MRI scoring systems	65.4 (19.1)
	5. Explore the relationship between observable features on MRI and symptoms, disease progression and treatment response	71.2 (21.9)
Epidemiology	6. Develop consensus on the components of pain variables to be included in the definition of symptomatic OA (i.e., descriptors, duration, location)	75.9 (25.5)
	7. Develop criteria to document radiographic progression	74.7 (20.4)
	8. Determine whether ankle OA is a separate entity to foot OA	70.2 (23.5)
	9. Identify whether foot and ankle OA phenotypes change over time	73.7 (17.3)
Burden	10. Examine progression of foot and ankle OA and mechanical function through longitudinal investigations in diverse populations	74.4 (20.0)
	11. Advance the understanding of consequent effects of early, mid and late-stage ankle OA and midfoot OA on mechanical function using gait analysis with 3D kinematics	64.4 (18.8)
	12. Clarify differences between health-related quality of life among those with and without foot and ankle OA	74.9 (24.8)
	13. Determine subgroup-specific approaches to improve health-related quality of life related to foot and ankle OA	74.2 (18.0)
Outcome assessment	14. Quantify the economic and societal burden of foot and ankle OA	85.3 (16.7)
	15. Work parallel with OMERACT to develop an agreed, standardised core outcome set for foot and ankle OA, including patient-reported outcome measures, physical function and structural measures	82.3 (27.5)
	16. Further evaluate the measurement properties of existing patient-reported outcome measures for foot and ankle OA	75.4 (22.9)
	17. Development of new foot and ankle OA-specific patient-reported outcome measures	64.2 (28.0)
Treatment	18. Further validation of ultrasound and MRI imaging-specific outcome measures to assess inflammatory features and structural damage in foot and ankle OA	70.0 (24.3)
	19. Ascertain what usual care is for foot and ankle OA so it can be used as the comparator in clinical trials	82.9 (15.6)
	20. Identify appropriate placebos/shams for use in clinical trials	69.2 (21.1)
	21. Evaluate the efficacy of exercise in the treatment of foot and ankle OA	82.8 (18.7)
	22. Evaluate the efficacy of weight loss in the treatment of foot and ankle OA	74.0 (22.7)
	23. Evaluate the efficacy of orthoses and footwear in the treatment of foot and ankle OA	79.1 (19.3)
	24. Develop models of care for foot and ankle OA that can be implemented in general practice	88.4 (11.5)

Table II

Osteoarthritis and Cartilage

Mean (SD) scores for each research agenda item from the symposium delegates ($n = 31$). Bolded items met the prespecified criteria of ≥ 70

In the foot, clinical diagnostic criteria are scarce. One previous study developed a clinical diagnostic rule for identifying radiographic first MTP joint OA²⁹. The presence of longstanding pain, a palpable dorsal joint osteophyte, crepitus, hard end-feel and restricted range of motion had good diagnostic accuracy for identifying radiographic OA, with excellent sensitivity and specificity.

Clinical diagnosis of midfoot OA is more difficult. The midfoot joints are in close proximity, making it challenging to isolate and assess for tenderness, stiffness, and deformity. Clinical assessments comprising foot posture, range of motion and palpable dorsal osteophytes performed poorly for identifying radiographic OA in people with midfoot pain³⁰. Diagnosis of midfoot OA remains reliant on palpation or provocation of the suspected joint in conjunction with diagnostic imaging, most commonly plain radiographs. Injection with local anaesthetic to determine which joints are symptomatic is possible, but the utility is questionable given the small joint spaces and possibility of leakage into adjacent joints³¹. Whilst some provocation tests assess the integrity of the midfoot joints following Lisfranc injury^{32,33}, there is a lack of specific and validated clinical tests for assessing the presence of OA in the midfoot. For example, the 'piano key' test³⁴ has been described, however its diagnostic performance is undetermined.

There is no clinical definition for ankle OA. Consequently, clinicians typically use a range of clinical signs and symptoms, with or without imaging, to form a diagnosis³⁵. Uniquely, most ankle OA cases are considered post-traumatic³⁶. Thus, there are calls to consider post-traumatic ankle OA as a distinct entity³⁷, possibly requiring a separate clinical definition.

Research agenda

- Develop an overarching clinical definition of foot and ankle OA
- Develop clinical diagnostic criteria for midfoot and ankle OA
- Explore the relationship between observable features and symptoms, disease progression and treatment response

Epidemiology

Definitions of foot and ankle OA in epidemiological studies

Epidemiological studies have employed various definitions of rOA and srOA to estimate prevalence and incidence (Table III).

Prevalence of foot and ankle OA

There are more prevalence estimates for foot OA than ankle OA, and more for rOA than srOA. In the Johnston County Osteoarthritis Study (JoCoOA), the prevalence of foot rOA was 22%³⁸. The prevalence of foot srOA was 5%^{38,39}, whilst in the Clinical Assessment Study of the Foot (CASF), it was 17% in adults aged ≥ 50 years⁴⁰. First MTP joint rOA prevalence was 10% in JoCoOA³⁹, 8% in the Clearwater OA Study⁴¹, and ranged from <4% in the 20 to 24 age group to approximately one-half of over 80s in the Zoetermeer study⁴². In CASF, first MTP joint srOA affected 8%²⁷. In the Zoetermeer study, tarsometatarsal rOA prevalence ranged from <1% in people aged 20–24 years to >7% in the over 80s⁴². The second cuneometatarsal joint is more commonly affected by rOA and srOA than other midfoot joints. The prevalence of rOA at the first cuneometatarsal, second cuneometatarsal, navicular-first cuneiform, and talonavicular joints

Study	n	Age range (mean)	% female	Population	Country	Radiographic views	Joints assessed	Grading system	Radiographic definition	Symptomatic definition
Zoetermeer Study	6,585	19+ (NR)	53	Zoetermeer, Western Netherlands	Netherlands	NR	First to fifth MTP, TMT, PIP	KL	Grade ≥ 2	—
Clearwater Osteoarthritis Study	3,436	40–94 (62)	>69	Pinellas County, Florida	USA	WB AP	First MTP	KL	Grade ≥ 2	—
Clinical Assessment Study of the Foot	525	50–87 (65)	56	4 general practices, North Staffordshire	UK	WB AP WB lateral	First MTP, first CM, second CM, NC, TNJ	La Trobe Foot Atlas	Grade ≥ 2 for OP and/or JSN, either view	Pain in past 4 weeks in corresponding region of the foot
Johnston County Osteoarthritis Project	863	55+ (71)	68	6 communities in Johnston County, North Carolina	USA	WB AP WB lateral	First MTP, first CM, second CM, NC, TNJ	La Trobe Foot Atlas	Grade ≥ 2 for OP and/or JSN, either view	Pain, aching or stiffness in corresponding foot
Chingford Study	209	45–64 (57)	100	1 general practice, Chingford, East London	UK	Semi-WB AP	First MTP	La Trobe Foot Atlas	Grade ≥ 2 for OP and/or JSN	—

NR: not reported; KL: Kellgren and Lawrence; MTP: metatarsophalangeal; TMT: tarsometatarsal; PIP: proximal interphalangeal; CM: cuneometatarsal; NC: navicular-first cuneiform; TN: talonavicular; WB: weightbearing; AP: antero-posterior; OP: osteophytes; JSN: joint space narrowing.

Table III

Osteoarthritis and Cartilage

Characteristics of key epidemiology studies reporting prevalence and incidence of foot and ankle OA

was 3%, 7%, 5%, and 6% respectively in JoCoOA³⁹, but substantially higher (22.9%, 65.4%, 39.5% and 35.6%, respectively) in older adults (mean age 76 years) in Australia⁴³. In CASF, the prevalence of midfoot srOA was 12% overall, and 3.9%, 6.8%, 5.2%, and 5.8% respectively at the same individual joints^{27,44}. Prevalence was 2% for ankle rOA in JoCoOA³⁹ and 3.4% for ankle srOA in CASF⁶.

Incidence of foot and ankle OA

There are few studies of foot and ankle OA incidence. Over 3–4 years in JoCoOA, 4% of participants developed incident foot rOA⁴⁵, and 28% incident ankle rOA over 4–5 years. Over seven years, in the Clearwater OA Study, approximately one-quarter developed first MTP joint rOA⁴⁶. In the Chingford study, 13.5% developed incident rOA in the right first MTP joint and 8.3% in the left over 19 years⁴⁷.

Phenotypes

In CASF, three distinct rOA phenotypes were distinguished: no or minimal foot OA (64%), isolated first MTP joint OA (22%) and polyarticular foot OA (15%)⁴⁸. Isolated medial midfoot (talonavicular, navicular-first cuneiform or first cuneometatarsal joints) rOA was more common than isolated central (second cuneometatarsal joint) midfoot rOA only or combined medial and central midfoot rOA⁴⁹. Neither study explored the involvement of ankle OA in these phenotypes.

Risk factors

Most studies of risk factors for foot and ankle OA are cross-sectional, with few prospective studies. Older age and female sex are risk factors for foot rOA and srOA^{6,27,38,44,48,50}. Obesity was associated with presence of foot, first MTP joint and polyarticular foot rOA and midfoot srOA^{38,44,48,50}, but not severity of first MTP joint rOA⁵¹. In JoCoOA, foot rOA was more common in African Americans³⁸. Routine/manual occupations were associated with srOA in the foot²⁷ and midfoot⁴⁴ in CASF. First MTP joint rOA was associated with

occupational stair-climbing in men in the Clearwater study⁵⁰ but not with lifetime occupation in the Chingford cohort⁵².

Pronated foot posture is associated with incident first MTP joint rOA⁴⁶, talonavicular and navicular-first cuneiform rOA⁴³ and midfoot srOA³⁰. People with midfoot OA have weaker foot and lower limb muscles (srOA) compared with asymptomatic controls⁴⁰ and an association between talonavicular rOA and knee hypermobility was found in JoCoOA³⁹. Foot OA co-occurs with OA at other joint sites. Hand and knee rOA is more common in people with foot and first MTP joint OA⁴¹, and hand rOA in polyarticular foot rOA⁴⁸. Midfoot srOA is associated with OA in the lower limb but not finger interphalangeal joints⁴⁴.

In JoCoOA and CASF, ankle srOA was associated with younger age, female sex, routine/manual occupations, and knee hypermobility^{6,39}.

Prognosis

Few prospective studies have examined the prognosis of foot or ankle OA. In CASF, there were small reductions in foot pain severity over 18 months⁵³. In JoCoOA, radiographic progression occurred in 55% of those with baseline foot rOA and 16% of those had ipsilateral foot symptoms at follow-up. Being female and having higher body mass index (BMI) were associated with incident foot rOA, while gout was associated with both incidence and progression. Previous injury was related to foot rOA with symptoms, but not foot rOA alone. Work disability, BMI and gout were associated with worsening in several Foot and Ankle Outcome Score (FAOS) subscales including pain, other symptoms, activities of daily living, sport and recreation function and foot and ankle-related quality of life⁴⁵.

In the Chingford study, progression of first MTP joint rOA occurred in 30% of first MTP joints over 19 years. Incidence and progression were more evident in the right first MTP joint and were driven by osteophytes, and unilateral involvement progressed to bilateral in one-third of women⁴⁷.

In JoCoOA, 37% of those with ankle rOA had symptomatic worsening in the FAOS symptoms subscale and 7% had worsening of ankle symptoms over 3–4 years. Among ankles with baseline rOA, 4% had progressive rOA, associated with prior ankle injury and concomitant foot or knee OA. Symptomatic worsening was associated with smoking, higher BMI, and additional symptomatic joints⁵⁴.

Research agenda

- Develop consensus on the components of pain variables to be included in the definition of symptomatic OA (i.e., descriptors, duration, location)
- Develop criteria to document radiographic progression
- Determine whether ankle OA is a separate entity to foot OA
- Identify whether foot and ankle OA phenotypes change over time

Burden

Symptoms and impairments

Foot OA is an important contributor to the burden of OA and has a significant impact on mobility^{27,44}. Most investigations relate to the first MTP joint and ankle joint, with less known about midfoot OA.

First MTP joint OA is associated with decreased range of first MTP joint dorsiflexion⁵⁵ and increased plantar pressure under the hallux and lesser toes^{56–58}. Consequently, individuals with first MTP joint OA adopt pain avoidance gait patterns^{59–61}. These may contribute to the development of secondary calluses and interphalangeal joint hyperextension^{51,56,62}. These investigations are comparative cross-sectional observations with mostly small sample sizes. Only one reports from a large population sample, the MOST study⁵⁹ ($n = 1,693$), although this is also cross-sectional.

Midfoot OA results in significant impairment of daily activity¹¹. Midfoot OA is associated with reduced foot and leg muscle strength⁴⁰, difficulty in walking⁴⁸ and climbing stairs⁶³. Individuals with midfoot OA have flatter feet and higher midfoot plantar pressures during barefoot walking, and these plantar pressures correlate with pain severity^{43,44,64}. Findings from CASF suggest mechanical loading may play an important role in the aetiology of symptomatic and structural midfoot OA and are important modifiable mediators of onset and progression⁴⁴. Similar to the first MTP joint, these investigations are cross-sectional, however three are derived from larger population samples ($n = 533$ ¹⁵, $n = 205$ ¹², $n = 525$ ¹³).

Ankle OA is common and presents a significant burden, with ankle pain accounting for 10% of musculoskeletal-related consultations in UK primary care⁶⁵. Physical impairment associated with ankle OA has been reported to be equivalent to end-stage kidney disease and congestive heart failure^{66–68}. Individuals with ankle OA have significant deficiencies in gait, persistent instability, reduced stability during stair climbing, worse postural control, greater reported disability, and altered plantar pressure^{69–73}. Those with asymmetric or unilateral ankle OA demonstrate atrophy and reduced activation of lower leg muscles^{74–77}.

Health-related quality of life (HRQoL)

Foot and ankle OA has a substantial impact on HRQoL. People with first MTP joint srOA have significantly worse foot-specific HRQoL than matched controls in all domains of the Foot Health Status Questionnaire (FHSQ), indicating greater foot pain, worse foot function, difficulty with finding appropriate footwear, and poorer general foot health. Furthermore, general HRQoL was significantly worse for cases than controls based on the Short

Form–36 Health Survey (SF-36) physical function domain scores⁷⁸. Compared to people without ankle symptoms, those with ankle srOA had lower HRQoL, suggesting that quality of life is influenced more by symptoms than radiographic disease⁷⁹. Former professional football and rugby players with a diagnosis of ankle OA have also been shown to have poorer HRQoL scores for physical health⁸⁰.

A general approach to improving HRQoL may not be effective for all people with lower body OA. Lower educational status was related to worse scores for SF-36 HRQoL domains of general health, mental health, and social functioning among patients with foot or ankle OA⁸¹. Compared to patients with knee OA, obesity was linked to poorer scores for HRQoL domains of social functioning, body pain, and general health among patients with foot or ankle OA⁸¹. This suggests that those who are of lower educational status or are obese with foot or ankle OA may need specific approaches to improve overall HRQoL that differ from knee OA.

Economic and societal burden

The economic and societal burden has not been quantified specifically for foot and ankle OA, but this is likely comparable to OA elsewhere due to its high prevalence and associated treatment costs, work-related costs, and disability⁸². Healthcare costs related to foot or ankle OA may be lessened with self-care and conservative management models. For example, in an analysis of Australian general practice data⁸³, OA of the foot or ankle was primarily managed with analgesic medications, while non-pharmacologic approaches and allied health referrals less frequent.

Research agenda

- Quantify the economic and societal burden of foot and ankle OA
- Clarify differences between HRQoL among those with and without foot and ankle OA
- Examine progression of foot and ankle OA and mechanical function through longitudinal investigations in diverse populations
- Determine subgroup-specific approaches to improve HRQoL related to foot and ankle OA

Outcome assessment

There is no consensus on what outcome domains should be measured in foot and ankle OA, or which instruments should be used. An Outcome Measures in Rheumatology (OMERACT) core set of outcome measures for foot and ankle disorders in rheumatic and musculoskeletal diseases, including foot and ankle OA, is in development.

Patient-reported outcome measures (PROMs)

No PROMs have been developed specifically for foot and/or ankle OA. The most frequently used PROMs in trials of people with foot OA are either generic or intended for general foot and ankle disorders. Primary outcome measures have included visual analogue or numeric rating scales for pain^{84–86}, the FHSQ pain domain^{87–89}, the Manchester Foot Pain and Disability Index function subscale⁸⁶, and the Foot and Ankle Ability Measure (FAAM) sport score⁸⁵.

The Ankle Osteoarthritis Scale (AOS) is the only PROM specifically developed for ankle OA. In a Cochrane review of non-surgical treatments for ankle OA, three of the six included trials used the AOS as a primary outcome measure⁹⁰. Other outcome measures used in ankle OA trials include the American Orthopaedic Foot and Ankle Society (AOFAS) score⁹¹ and visual analogue score (VAS) for pain⁹², whilst an ongoing trial comparing ankle replacement surgery to ankle arthrodesis has specified the Manchester–Oxford

Foot Questionnaire (MOXFQ) walking/standing domain score as the primary outcome measure⁹³.

There has been limited evaluation of the measurement properties of many of these PROMs in foot and ankle OA populations⁹⁴. High responsiveness has been observed for the FHSQ pain subscale, Foot Function Index-Revised (FFI-R) short form pain subscale and 100 mm VAS of walking pain severity in individuals with first MTP joint OA⁹⁵, and acceptable responsiveness has been reported for the AOFAS, Self-reported Foot and Ankle Score (SEFAS) and FAOS in individuals undergoing surgery for ankle OA^{96–98}. A recent review recommended the use of the FFI-R, FHSQ or MOXFQ for clinical trials of general foot disorders and the MOXFQ or SEFAS for foot surgery, but no recommendations were made specifically for trials of foot and ankle OA⁹⁹. Further evaluation of the broader psychometric properties of PROMs in foot and ankle OA populations is needed.

Physical performance measures

There are currently no recommendations on which physical performance measures should be used for individuals with foot and ankle OA. Objective measures of function have typically been specified as secondary outcome measures in foot and ankle OA studies; including muscle strength^{84,87}, kinetics^{86,87} and kinematics^{84,87,89,93}. The AOFAS Score also contains objective, clinician-mediated measures of function, including sagittal motion. The Single Leg Stance test and Timed Up and Go test have been used to measure physical performance in ankle OA¹⁰⁰.

Goniometric measurements of range of motion are reliable and valid in measuring first MTP joint²⁹ and ankle joint¹⁰¹ OA. However, the measurement properties of instruments used to assess muscle strength, and of the Single Leg Stance and Timed Up and Go tests, have not been evaluated in foot and ankle OA cohorts. Use of the AOFAS Score has been discouraged as it is neither reliable nor valid^{94,99}. Consensus on which physical performance measures should be used in foot and ankle OA is required.

Structural outcome measures

Recent European Alliance of Associations for Rheumatology (EULAR) recommendations for the use of imaging of peripheral joint OA acknowledged a paucity of research concerning foot OA and recommended more studies¹⁰². Conventional radiography has traditionally been used to assess the severity of OA, although there is increasing interest in the use of imaging modalities such as MRI, ultrasound, and CT. Further validation of these scoring systems is necessary.

Research agenda

- Work parallel with OMERACT to develop an agreed, standardised core outcome set for foot and ankle OA, including PROMs, physical function and structural measures
- Further evaluate the measurement properties of existing PROMs for foot and ankle OA
- Further validation of US and MRI imaging-specific outcome measures to assess inflammatory lesions and structural damage in foot and ankle OA

Treatment

There are a limited number of randomised clinical trials (RCTs) that have evaluated interventions for foot and ankle OA and no clinical consensus guidelines. Thus, at present, there is limited evidence to guide management.

Weight loss

There is evidence obesity is associated with foot pain¹⁰³ and that weight loss can improve foot pain^{104,105}, but no RCTs have investigated the efficacy of weight loss interventions for foot and ankle OA.

Devices including footwear, ankle orthoses and foot orthoses

Two RCTs^{88,106} have investigated the efficacy of footwear and foot orthoses for first MTP joint OA. Menz *et al.*⁸⁸ compared prefabricated foot orthoses to rocker-sole shoes in individuals with first MTP joint OA. Both groups improved, but there were no significant between-group differences for foot pain or function at 12 weeks. Munteanu *et al.*⁸⁹ compared shoe-stiffening inserts to sham shoe inserts. Foot pain and function were improved in the shoe-stiffening insert group at all time points up to 52 weeks. An ongoing RCT is comparing arch contouring foot orthoses to flat insoles for first MTP joint OA¹⁰⁷.

There are no RCTs of the efficacy of orthotic devices for midfoot, hindfoot or ankle OA. One study⁸⁶ explored the feasibility of an RCT of contoured foot orthoses compared to sham flat insoles for midfoot OA. Further fully-powered studies are needed.

Physical therapy

One RCT⁸⁴ investigated the efficacy of adding sesamoid mobilisation, flexor hallucis longus strengthening and gait training to a physical therapy program for first MTP joint OA. At 4 weeks, there was a significant difference between groups for pain in favour of the added interventions. Another trial evaluated the efficacy of physical therapy combined with corticosteroid injection or corticosteroid injection alone in individuals with ankle joint OA¹⁰⁸. At 28 days, pain and HRQoL were significantly improved in the combined intervention group.

Pharmacological interventions

Few studies have evaluated pharmacological interventions. One RCT¹⁰⁹ that included the foot and other OA sites, compared ozonated oil to placebo oil massaged twice daily on to the joint site. At 60 days, reductions in pain and function were shown in both groups, with no between-group differences.

For the first MTP joint, one RCT⁸⁷ found that a single intra-articular injection of hyaluronan (Hylan G-F 20, Synvisc®) was no more effective than placebo for foot pain or function over 6 months.

For ankle joint OA, three placebo-controlled trials examined hyaluronate (Hyalgan®¹¹⁰, unbranded¹¹¹ and Supartz®⁹¹) and reported inconsistent outcomes at 3 months. The main limitation of these studies were small sample sizes ($n = 30, 20$ and 64 , respectively). Further, there were dosage variations. Two trials^{110,111} used multiple dosing regimens (1 ml weekly injection for 5 weeks), whereas one⁹¹ used a single dose. There are two head-to-head RCTs. Karatosun *et al.*¹¹² compared Adant® hyaluronate injections (weekly for 3 weeks) to a 6-week exercise therapy program, finding improvements in pain in both groups at 12 months but no between-group differences. Similarly, there were no differences in pain and disability at 6 months between an intra-articular injection of botulinum toxin type A compared with an intra-articular injection of hyaluronate combined with 12 sessions of rehabilitation exercise, although within-group improvements were seen¹⁰⁰.

Surgery

Two RCTs comparing arthrodesis and arthroplasty have been conducted for first MTP joint OA. Comparison of arthrodesis to total joint arthroplasty at two¹¹³ and 15 years¹¹⁴ in individuals with first MTP joint OA showed a significant between-group difference in pain favouring arthrodesis at two and 15 years. Baumhauer *et al.*⁸⁵ compared hemi-arthroplasty (Cartiva®) to arthrodesis for first MTP

joint OA in a non-inferiority trial. The authors reported statistical equivalence for the difference between groups at two years.

For ankle OA, the main surgical options are fusion and total ankle replacement. In one trial, Norvell *et al.*¹¹⁵ compared total ankle arthroplasty with arthrodesis. At 6, 12 and 24 months, both interventions were associated with improvements in the FAAM and SF-36; however, there were several between-group differences in favour of arthroplasty. Other trials have been performed that have compared newer types of total ankle replacements. Wood *et al.*¹¹⁶, compared the Buechel-Pappas total ankle replacement to the Scandinavian Total Ankle Replacement. At 54 months, there were no between-group differences in pain or function (AOFAS Score). Similarly, Nunley *et al.*¹¹⁷ compared the Scandinavian Total Ankle Replacement to a fixed-bearing (Salto Talaris®) total ankle replacement. At 2 years, pain and function improved in both groups, but there were no between-group differences. Finally, Saltzman *et al.*¹¹⁸ compared anterior osteophyte removal followed by either fixed ankle distraction or ankle distraction permitting joint motion. At 26, 52 and 104 weeks, both groups improved, with a significant between-group difference in favour of ankle distraction permitting joint motion group at all time points.

Research agenda

- Develop models of care for foot and ankle OA that can be implemented in general practice
- Ascertain what usual care is for foot and ankle OA so it can be used as the comparator in clinical trials
- Evaluate the efficacy of exercise in the treatment of foot and ankle OA
- Evaluate the efficacy of orthoses and footwear in the treatment of foot and ankle OA
- Evaluate the efficacy of weight loss in the treatment of foot and ankle OA

Discussion

The objective of this study was to summarise the available evidence relating to the diagnosis, epidemiology, burden, outcome assessment and treatment of foot and ankle OA and to develop an agenda to guide future research. By conducting an extensive narrative literature review, we have identified key knowledge gaps related to foot and ankle OA, and combined with the input of expert clinicians and researchers, have developed a preliminary agenda which will provide the basis for future research to improve our understanding and clinical management of this common and disabling condition.

Despite research on foot and ankle OA receiving substantially less attention compared to other joints, the research agenda items developed in this study are similar to those developed for OA more broadly, particularly in relation to improving the understanding of natural history and progression, identification of phenotypes, and the evaluation of non-surgical, non-drug treatments^{119,120}. However, the identified need to develop an overarching clinical definition and diagnostic criteria for foot and ankle OA reflects the fact that although clinical definitions for OA at the knee²⁴, hip²⁵ and hand²⁶ have existed for decades, no such definition exists for foot and/or ankle OA.

Given that foot and ankle research is a relatively nascent and evolving discipline within the broader field of OA, this paper represents the first step towards the development of a more formal and structured approach to identifying research priorities and developing standardised approaches to diagnosis, assessment, and

treatment. As such, the limitations of the approach we have used need to be acknowledged. Firstly, due to the breadth of topics covered, we conducted a narrative rather than systematic review. However, further systematic reviews are planned to target specific topic areas in greater detail. Secondly, our agenda-setting exercise can only be considered preliminary, as we used a simple scoring method rather than consensus methodologies such as the Delphi technique. Future studies will extend on this work using more structured approaches.

In conclusion, this study has identified key knowledge gaps related to foot and ankle OA, and a preliminary agenda to guide future research planning has been developed. Implementation of this agenda will assist in improving the understanding and clinical management of this common and disabling condition, thereby improving clinical outcomes.

Contributions

HBM, ER, CJB, MTH, KLP and LAG conceived the study. All authors drafted sections of the manuscript, revised the manuscript critically for important intellectual content, and read and approved the final version. All authors agree to be accountable for all aspects of the work.

Conflict of interest

None of the authors has a competing interest to declare.

Funding support

HBM is supported by a National Health and Medical Research Council of Australia Senior Research Fellowship (#1135993). KLP is supported by a National Health and Medical Research Council of Australia Emerging Leadership Investigator Grant (#1174229). MJT is supported by a National Institute for Health Research (NIHR) Development and Skills Enhancement Award (NIHR300818). The views expressed in this publication are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

Acknowledgements

We would like to sincerely thank the Osteoarthritis Research Society International (OARSI) for supporting the development of IFOAC and for hosting the virtual discussion group underpinning this work at the OARSI World Congress in May 2021, and administrative support from the Centre for Sport, Exercise and Osteoarthritis Research Versus Arthritis. We would like to thank all participants in the consensus meeting and survey. The following participants provided consent to be acknowledged as contributors: Michael Backhouse (University of Warwick, UK), Claire Brockett (University of Leeds, UK), T. Mark Campbell (Elisabeth Bruyère Hospital, Canada), Lindsey Cherry (University of Southampton, UK), Gabriel Gijon-Nogueron, University of Malaga, Spain), Tiffany K. Gill (University of Adelaide, Australia), Philip Helliwell (University of Leeds, UK), Kyle Benjamin Kosik (University of Kentucky, USA), Amy L. Lenz (University of Utah, USA), Polly Lim (La Trobe University, Australia), Marienke van Middelkoop (Erasmus MC University Medical Centre, The Netherlands), Thomas Perry (University of Oxford, UK), Miklós Pozsgai (Hungary), Erik A Wikstrom (University of North Carolina at Chapel Hill, USA), Richard A. Wilkins (University of Leeds, UK), Robert Wonink (Bergman Clinics, The Netherlands), Narelle Wyndow (University of Queensland, Australia).

References

- Roddy E, Menz HB. Foot osteoarthritis: latest evidence and developments. *Ther Adv Musculoskelet Dis* 2018;10:91–103.
- Golightly YM, Gates LS. Foot osteoarthritis: addressing an overlooked global public health problem. *Arthritis Care Res* 2021;73:767–9.
- Trivedi B, Marshall M, Belcher J, Roddy E. A systematic review of radiographic definitions of foot osteoarthritis in population-based studies. *Osteoarthritis Cartilage* 2010;18:1027–35.
- Zammit GV, Menz HB, Munteanu SE, Landorf KB, Gilheany MF. Interventions for treating osteoarthritis of the big toe joint. *Cochrane Database Syst Rev* 2010, CD007809.
- Lithgow MJ, Munteanu SE, Buldt AK, Arnold JB, Kelly LA, Menz HB. Foot structure and lower limb function in individuals with midfoot osteoarthritis: a systematic review. *Osteoarthritis Cartilage* 2020;28:1514–24.
- Murray C, Marshall M, Rathod T, Bowen CJ, Menz HB, Roddy E. Population prevalence and distribution of ankle pain and symptomatic radiographic ankle osteoarthritis in community dwelling older adults: a systematic review and cross-sectional study. *PLoS One* 2018;13, e0193662.
- Patel A, Rao S, Nawoczenski D, Flemister AS, DiGiovanni B, Baumhauer JF. Midfoot arthritis. *J Am Acad Orthop Surg* 2010;18:417–25.
- Verhoeven N, Vandeputte G. Midfoot arthritis: diagnosis and treatment. *Foot Ankle Surg* 2012;18:255–62.
- Kalichman L, Hernandez-Molina G. Midfoot and forefoot osteoarthritis. *Foot* 2014;24:128–34.
- Paterson KL, Gates L. Clinical assessment and management of foot and ankle osteoarthritis: a review of current evidence and focus on pharmacological treatment. *Drugs Aging* 2019;36:203–11.
- Kurup H, Vasukutty N. Midfoot arthritis- current concepts review. *J Clin Orthop Trauma* 2020;11:399–405.
- Kellgren JH, Lawrence JS. Radiological assessment of osteoarthritis. *Ann Rheum Dis* 1957;16:494–502.
- Cicuttini FM, Spector TD. The epidemiology of osteoarthritis of the hand. *Rev Rhum Engl Ed* 1995;62:35.
- Spector T, Hart D, Byrne J, Harris P, Dacre J, Doyle D. Definition of osteoarthritis of the knee for epidemiological studies. *Ann Rheum Dis* 1993;52:790.
- Menz HB, Munteanu SE, Landorf KB, Zammit GV, Cicuttini FM. Radiographic classification of osteoarthritis in commonly affected joints of the foot. *Osteoarthritis Cartilage* 2007;15:1333–8.
- Kraus VB, Kilfoil TM, Hash 2nd TW, McDaniel G, Renner JB, Carrino JA, *et al.* Atlas of radiographic features of osteoarthritis of the ankle and hindfoot. *Osteoarthritis Cartilage* 2015;23:2059–85.
- Munteanu SE, Auhl M, Tan JM, Landorf KB, Elzarka A, Tan B, *et al.* Development and reproducibility of a first metatarsophalangeal joint osteoarthritis magnetic resonance imaging scoring system. *Arthritis Care Res* 2020;72:1205–12.
- Munteanu SE, Auhl M, Tan JM, Landorf KB, Elzarka A, Menz HB. Characterisation of first metatarsophalangeal joint osteoarthritis using magnetic resonance imaging. *Clin Rheumatol* 2021;40:5067–76.
- Zaidi R, Hargunani R, Calleja M, Foley J, Goldberg A. MRI classification of subtalar joint osteoarthritis using a novel scoring system. *Open J Radiol* 2020;10:69.
- Halstead J, Martín-Hervás C, Hensor EMA, McGonagle D, Keenan A-M, Redmond AC, *et al.* Development and reliability of a preliminary foot osteoarthritis magnetic resonance imaging score. *J Rheumatol* 2017;44:1257–64.
- Aboelmagd S. MRI Scoring of Osteoarthritis of the Ankle. Norwich Medical School. Doctor of Medicine: University of East Anglia; 2016.
- Zabotti A, Filippou G, Canzoni M, Adinolfi A, Picerno V, Carrara G, *et al.* OMERACT agreement and reliability study of ultrasonographic elementary lesions in osteoarthritis of the foot. *RMD Open* 2019;5, e000795.
- Lintz F, Beaudet P, Richardi G, Brillhault J. Weight-bearing CT in foot and ankle pathology. *Orthop Traumatol Surg Res* 2021;107:102772.
- Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, *et al.* Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. *Arthritis Rheum* 1986;29:1039–49.
- Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K, *et al.* The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. *Arthritis Rheum* 1991;34:505–14.
- Altman R, Alarcon G, Appelrouth D, Bloch D, Borenstein D, Brandt K, *et al.* The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. *Arthritis Rheum* 1990;33:1601–10.
- Roddy E, Thomas MJ, Marshall M, Rathod T, Myers H, Menz HB, *et al.* The population prevalence of symptomatic radiographic foot osteoarthritis in community-dwelling older adults: cross-sectional findings from the clinical assessment study of the foot. *Ann Rheum Dis* 2015;74:156–63.
- Paterson KL, Arnold JB. A defined problem: working towards a clinical definition of foot osteoarthritis. *Arthritis Care Res* 2021;73:1228–30.
- Zammit GV, Munteanu SE, Menz HB. Development of a diagnostic rule for identifying radiographic osteoarthritis in people with first metatarsophalangeal joint pain. *Osteoarthritis Cartilage* 2011;19:939–45.
- Thomas MJ, Roddy E, Rathod T, Marshall M, Moore A, Menz HB, *et al.* Clinical diagnosis of symptomatic midfoot osteoarthritis: cross-sectional findings from the Clinical Assessment Study of the Foot. *Osteoarthritis Cartilage* 2015;23:2094–101.
- Endo Y, Nwawka OK, Smith S, Burket JC. Tarsometatarsal joint communication during fluoroscopy-guided therapeutic joint injections and relationship with patient age and degree of osteoarthritis. *Skeletal Radiol* 2018;47:271–7.
- Shapiro MS, Wascher DC, Finerman GAM. Rupture of lisfranc's ligament in athletes. *Am J Sports Med* 1994;22:687–91.
- Myerson MS, Cerrato RA. Current management of tarsometatarsal injuries in the athlete. *J Bone Joint Surg* 2008;90:2522–33.
- Keiserman LS, Cassandra J, Amis JA. The piano key test: a clinical sign for the identification of subtle tarsometatarsal pathology. *Foot Ankle Int* 2003;24:437–8.
- Barg A, Pagenstert GI, Hugle T, Gloyer M, Wiewiorski M, Henninger HB, *et al.* Ankle osteoarthritis: etiology, diagnostics, and classification. *Foot Ankle Clin* 2013;18:411–26.
- Saltzman CL, Salamon ML, Blanchard GM, Huff T, Hayes A, Buckwalter JA, *et al.* Epidemiology of ankle arthritis: report of a consecutive series of 639 patients from a tertiary orthopaedic center. *Iowa Orthop J* 2005;25:44.
- Delco ML, Kennedy JG, Bonassar LJ, Fortier LA. Post-traumatic osteoarthritis of the ankle: a distinct clinical entity requiring new research approaches. *J Orthop Res* 2017;35:440–53.
- Flowers P, Nelson AE, Hannan MT, Hillstrom HJ, Renner JB, Jordan JM, *et al.* Foot osteoarthritis frequency and associated factors in a community-based cross-sectional study of White and African American adults. *Arthritis Care Res* 2021;73:1784–8.

39. Golightly YM, Hannan MT, Nelson AE, Hillstrom HJ, Cleveland RJ, Kraus VB, *et al.* Relationship of joint hypermobility with ankle and foot radiographic osteoarthritis and symptoms in a community-based cohort. *Arthritis Care Res* 2019;71:538–44.
40. Arnold JB, Halstead J, Grainger AJ, Keenan AM, Hill CL, Redmond AC. Foot and leg muscle weakness in people with midfoot osteoarthritis. *Arthritis Care Res* 2021;73:772–80.
41. Wilder FV, Barrett JP, Farina EJ. The association of radiographic foot osteoarthritis and radiographic osteoarthritis at other sites. *Osteoarthritis Cartilage* 2005;13:211–5.
42. van Saase J, van Romunde LK, Cats A, Vandenbroucke JP, Valkenburg HA. Epidemiology of osteoarthritis: Zoetermeer survey. Comparison of radiological osteoarthritis in a Dutch population with that in 10 other populations. *Ann Rheum Dis* 1989;48:271–80.
43. Menz HB, Munteanu SE, Zammit GV, Landorf KB. Foot structure and function in older people with radiographic osteoarthritis of the medial midfoot. *Osteoarthritis Cartilage* 2010;18:317–22.
44. Thomas MJ, Peat G, Rathod T, Marshall M, Moore A, Menz HB, *et al.* The epidemiology of symptomatic midfoot osteoarthritis in community-dwelling older adults: cross-sectional findings from the Clinical Assessment Study of the Foot. *Arthritis Res Ther* 2015;17:178.
45. Eltaraboulsi RNA, Alvarez C, Renner J, Bowen C, Gates L, Golightly Y. Incidence and progression of foot osteoarthritis [abstract]. *Arthritis Rheumatol* 2020:72.
46. Mahiquez MY, Wilder FV, Stephens HM. Positive hindfoot valgus and osteoarthritis of the first metatarsophalangeal joint. *Foot Ankle Int* 2006;27:1055–9.
47. Bowen C, Gates L, McQueen P, Daniels M, Delmestri A, Drechsler W, *et al.* Natural history of radiographic first metatarsophalangeal joint osteoarthritis: a nineteen-year population-based cohort study. *Arthritis Care Res* 2020;72:1224–30.
48. Rathod T, Marshall M, Thomas MJ, Menz HB, Myers HL, Thomas E, *et al.* Investigations of potential phenotypes of foot osteoarthritis: cross-sectional analysis from the clinical assessment study of the foot. *Arthritis Care Res* 2016;68:217–27.
49. Arnold JB, Marshall M, Thomas MJ, Redmond AC, Menz HB, Roddy E. Midfoot osteoarthritis: potential phenotypes and their associations with demographic, symptomatic and clinical characteristics. *Osteoarthritis Cartilage* 2019;27:659–66.
50. Bernard TE, Wilder FV, Aluoch M, Leaverton PE. Job-related osteoarthritis of the knee, foot, hand, and cervical spine. *J Occup Environ Med* 2010;52:33–8.
51. Menz HB, Roddy E, Marshall M, Thomas MJ, Rathod T, Myers H, *et al.* Demographic and clinical factors associated with radiographic severity of first metatarsophalangeal joint osteoarthritis: cross-sectional findings from the Clinical Assessment Study of the Foot. *Osteoarthritis Cartilage* 2015;23:77–82.
52. Cherry L, Gates L, Arden NK, Bowen CJ. Lifetime occupation is not associated with radiographic osteoarthritis of the first metatarsophalangeal joint in a cohort study of UK women. *J Foot Ankle Res* 2020;13:61.
53. Downes TJ, Chesterton L, Whittle R, Roddy E, Menz HB, Marshall M, *et al.* Symptomatic course of foot osteoarthritis phenotypes: an 18-month prospective analysis of community-dwelling older adults. *Arthritis Care Res* 2018;70:1107–12.
54. Jaleel A, Golightly YM, Alvarez C, Renner JB, Nelson AE. Incidence and progression of ankle osteoarthritis: the johnston county osteoarthritis project. *Semin Arthritis Rheum* 2021;51:230–5.
55. Halstead J, Redmond AC. Weight-bearing passive dorsiflexion of the hallux in standing is not related to hallux dorsiflexion during walking. *J Orthop Sports Phys Ther* 2006;36:550–6.
56. Zammit GV, Menz HB, Munteanu SE, Landorf KB. Plantar pressure distribution in older people with osteoarthritis of the first metatarsophalangeal joint (hallux limitus/rigidus). *J Orthop Res* 2008;26:1665–9.
57. Van Gheluwe B, Dananberg HJ, Hagman F, Vanstaen K. Effects of hallux limitus on plantar foot pressure and foot kinematics during walking. *J Am Podiatr Med Assoc* 2006;96:428–36.
58. Bryant A, Tinley P, Singer K. Plantar pressure distribution in normal, hallux valgus and hallux limitus feet. *Foot* 1999;9:115–9.
59. Rao S, Gross KD, Niu J, Nevitt MC, Lewis CE, Torner JC, *et al.* Are pressure time integral and cumulative plantar stress related to first metatarsophalangeal joint pain? Results from a community-based study. *Arthritis Care Res* 2016;68:1232–8.
60. Menz HB, Auhl M, Tan JM, Buldt AK, Munteanu SE. Centre of pressure characteristics during walking in individuals with and without first metatarsophalangeal joint osteoarthritis. *Gait Posture* 2018;63:91–6.
61. Canseco K, Long J, Marks R, Khazzam M, Harris G. Quantitative characterization of gait kinematics in patients with hallux rigidus using the Milwaukee foot model. *J Orthop Res* 2008;26:419–27.
62. Menz HB, Zammit GV, Munteanu SE. Plantar pressures are higher under callused regions of the foot in older people. *Clin Exp Dermatol* 2007;32:375–80.
63. Rao S, Baumhauer JF, Tome J, Nawoczenski DA. Comparison of in vivo segmental foot motion during walking and step descent in patients with midfoot arthritis and matched asymptomatic control subjects. *J Biomech* 2009;42:1054–60.
64. Rao S, Baumhauer JF, Nawoczenski DA. Is barefoot regional plantar loading related to self-reported foot pain in patients with midfoot osteoarthritis. *Osteoarthritis Cartilage* 2011;19:1019–25.
65. Menz HB, Jordan KP, Roddy E, Croft PR. Characteristics of primary care consultations for musculoskeletal foot and ankle problems in the UK. *Rheumatology* 2010;49:1391–8.
66. Hubbard TJ, Hicks-Little C, Cordova M. Mechanical and sensorimotor implications with ankle osteoarthritis. *Arch Phys Med Rehabil* 2009;90:1136–41.
67. Khazzam M, Long JT, Marks RM, Harris GF. Preoperative gait characterization of patients with ankle arthrosis. *Gait Posture* 2006;24:85–93.
68. Saltzman CL, Zimmerman MB, O'Rourke M, Brown TD, Buckwalter JA, Johnston R. Impact of comorbidities on the measurement of health in patients with ankle osteoarthritis. *J Bone Joint Surg Am* 2006;88:2366–72.
69. Horisberger M, Hintermann B, Valderrabano V. Alterations of plantar pressure distribution in posttraumatic end-stage ankle osteoarthritis. *Clin Biomech* 2009;24:303–7.
70. Valderrabano V, Hintermann B, Horisberger M, Fung TS. Ligamentous posttraumatic ankle osteoarthritis. *Am J Sports Med* 2006;34:612–20.
71. Valderrabano V, Nigg BM, von Tschanner V, Stefanyshyn DJ, Goepfert B, Hintermann B. Gait analysis in ankle osteoarthritis and total ankle replacement. *Clin Biomech* 2007;22:894–904.
72. Wikstrom EA, Anderson RB. Alterations in gait initiation are present in those with posttraumatic ankle osteoarthritis: a pilot study. *J Appl Biomech* 2013;29:245–52.

73. Wikstrom EA, Anderson RB, Hubbard-Turner T. Alterations in stair ascent and descent kinetics are present in those with post-traumatic ankle osteoarthritis. *Int J Athl Ther Train* 2015;20:37–43.
74. Agel J, Coetzee JC, Sangeorzan BJ, Roberts MM, Hansen Jr ST. Functional limitations of patients with end-stage ankle arthrosis. *Foot Ankle Int* 2005;26:537–9.
75. Nuesch C, Huber C, Pagenstert G, von Tscharner V, Valderrabano V. Muscle activation of patients suffering from asymmetric ankle osteoarthritis during isometric contractions and level walking - a time-frequency analysis. *J Electromyogr Kinesiol* 2012;22:939–46.
76. Valderrabano V, von Tscharner V, Nigg BM, Hintermann B, Goepfert B, Fung TS, *et al.* Lower leg muscle atrophy in ankle osteoarthritis. *J Orthop Res* 2006;24:2159–69.
77. Wiewiorski M, Dopke K, Steiger C, Valderrabano V. Muscular atrophy of the lower leg in unilateral post traumatic osteoarthritis of the ankle joint. *Int Orthop* 2012;36:2079–85.
78. Bergin SM, Munteanu SE, Zammit GV, Nikolopoulos N, Menz HB. Impact of first metatarsophalangeal joint osteoarthritis on health-related quality of life. *Arthritis Care Res* 2012;64:1691–8.
79. Al-Mahrouqi MM, Vicenzino B, MacDonald DA, Smith MD. Disability, physical impairments, and poor quality of life, rather than radiographic changes, are related to symptoms in individuals with ankle osteoarthritis: a cross-sectional laboratory study. *J Orthop Sports Phys Ther* 2020;50:711–22.
80. Paget LDA, Aoki H, Kemp S, Lambert M, Readhead C, Stokes KA, *et al.* Ankle osteoarthritis and its association with severe ankle injuries, ankle surgeries and health-related quality of life in recently retired professional male football and rugby players: a cross-sectional observational study. *BMJ Open* 2020;10, e036775.
81. Perruccio AV, Gandhi R, Lau JT, Syed KA, Mahomed NN, Rampersaud YR. Cross-sectional contrast between individuals with foot/ankle vs knee osteoarthritis for obesity and low education on health-related quality of life. *Foot Ankle Int* 2016;37:24–32.
82. Zhao X, Shah D, Gandhi K, Wei W, Dwibedi N, Webster L, *et al.* Clinical, humanistic, and economic burden of osteoarthritis among noninstitutionalized adults in the United States. *Osteoarthritis Cartilage* 2019;27:1618–26.
83. Paterson KL, Harrison C, Britt H, Hinman RS, Bennell KL. Management of foot/ankle osteoarthritis by Australian general practitioners: an analysis of national patient-encounter records. *Osteoarthritis Cartilage* 2018;26:888–94.
84. Shamus J, Shamus E, Gugel RN, Brucker BS, Skaruppa C. The effect of sesamoid mobilization, flexor hallucis strengthening, and gait training on reducing pain and restoring function in individuals with hallux limitus: a clinical trial. *J Orthop Sports Phys Ther* 2004;34:368–76.
85. Baumhauer JF, Singh D, Glazebrook M, Blundell C, De Vries G, Le IL, *et al.* Prospective, randomized, multi-centered clinical trial assessing safety and efficacy of a synthetic cartilage implant versus first metatarsophalangeal arthrodesis in advanced hallux rigidus. *Foot Ankle Int* 2016;37:457–69.
86. Halstead J, Chapman GJ, Gray JC, Grainger AJ, Brown S, Wilkins RA, *et al.* Foot orthoses in the treatment of symptomatic midfoot osteoarthritis using clinical and biomechanical outcomes: a randomised feasibility study. *Clin Rheumatol* 2016;35:987–96.
87. Munteanu SE, Zammit GV, Menz HB, Landorf KB, Handley CJ, Elzarka A, *et al.* Effectiveness of intra-articular hyaluronan (Synvisc, hylan G-F 20) for the treatment of first metatarsophalangeal joint osteoarthritis: a randomised placebo-controlled trial. *Ann Rheum Dis* 2011;70:1838–41.
88. Menz HB, Auhl M, Tan JM, Levinger P, Roddy E, Munteanu SE. Effectiveness of foot orthoses versus rocker-sole footwear for first metatarsophalangeal joint osteoarthritis: randomized trial. *Arthritis Care Res* 2016;68:581–9.
89. Munteanu SE, Landorf KB, McClelland JA, Roddy E, Cicuttini FM, Shiell A, *et al.* Shoe-stiffening inserts for first metatarsophalangeal joint osteoarthritis: a randomised trial. *Osteoarthritis Cartilage* 2021;29:480–90.
90. Witteveen AG, Hofstad CJ, Kerkhoffs GM. Hyaluronic acid and other conservative treatment options for osteoarthritis of the ankle. *Cochrane Database Syst Rev* 2015, CD010643.
91. DeGroot 3rd H, Uzunishvili S, Weir R, Al-omari A, Gomes B. Intra-articular injection of hyaluronic acid is not superior to saline solution injection for ankle arthritis: a randomized, double-blind, placebo-controlled study. *J Bone Joint Surg Am* 2012;94:2–8.
92. Witteveen AG, Giannini S, Guido G, Jerosch J, Lohrer H, Vannini F, *et al.* A prospective multi-centre, open study of the safety and efficacy of hylan G-F 20 (Synvisc) in patients with symptomatic ankle (talo-crural) osteoarthritis. *Foot Ankle Surg* 2008;14:145–52.
93. Goldberg AJ, Zaidi R, Thomson C, Dore CJ, Skene SS, Cro S, *et al.* Total ankle replacement versus arthrodesis (TARVA): protocol for a multicentre randomised controlled trial. *BMJ Open* 2016;6, e012716.
94. Jia Y, Huang H, Gagnier JJ. A systematic review of measurement properties of patient-reported outcome measures for use in patients with foot or ankle diseases. *Qual Life Res* 2017;26:1969–2010.
95. Menz HB, Auhl M, Tan JM, Levinger P, Roddy E, Munteanu SE. Comparative responsiveness of outcome measures for the assessment of pain and function in first metatarsophalangeal joint osteoarthritis. *Arthritis Care Res* 2020;72:679–84.
96. Madeley NJ, Wing KJ, Topliss C, Penner MJ, Glazebrook MA, Younger AS. Responsiveness and validity of the SF-36, ankle osteoarthritis scale, AOFAS ankle hindfoot score, and foot function index in end stage ankle arthritis. *Foot Ankle Int* 2012;33:57–63.
97. Cöster M, Karlsson MK, Nilsson J, Carlsson A. Validity, reliability, and responsiveness of a self-reported foot and ankle score (SEFAS). *Acta Orthop* 2012;83:197–203.
98. Golightly YM, Devellis RF, Nelson AE, Hannan MT, Lohmander LS, Renner JB, *et al.* Psychometric properties of the foot and ankle outcome score in a community-based study of adults with and without osteoarthritis. *Arthritis Care Res* 2014;66:395–403.
99. Whittaker GA, Munteanu SE, Roddy E, Menz HB. Measures of foot pain, foot function, and general foot health. *Arthritis Care Res* 2020;72(Suppl 10):294–320.
100. Sun SF, Hsu CW, Lin HS, Chou YJ, Chen JY, Wang JL. Efficacy of intraarticular botulinum toxin A and intraarticular hyaluronate plus rehabilitation exercise in patients with unilateral ankle osteoarthritis: a randomized controlled trial. *J Foot Ankle Res* 2014;7:9.
101. Thornton J, Sabah S, Segaren N, Cullen N, Singh D, Goldberg A. Validated method for measuring functional range of motion in patients with ankle arthritis. *Foot Ankle Int* 2016;37: 868–73.
102. Sakellariou G, Conaghan PG, Zhang W, Bijlsma JWJ, Boyesen P, D'Agostino MA, *et al.* EULAR recommendations for the use of imaging in the clinical management of peripheral joint osteoarthritis. *Ann Rheum Dis* 2017;76:1484–94.

103. Butterworth PA, Landorf KB, Smith SE, Menz HB. The association between body mass index and musculoskeletal foot disorders: a systematic review. *Obes Rev* 2012;13:630–42.
104. Hooper MM, Stellato TA, Hallowell PT, Seitz BA, Moskowitz RW. Musculoskeletal findings in obese subjects before and after weight loss following bariatric surgery. *Int J Obes* 2007;31:114–20.
105. Morley WJ, Dawe E, Boyd R, Creasy J, Grice J, Marsland D, *et al.* Simulated weight reduction using an anti-gravity treadmill – a pilot study of the impact of weight loss on foot and ankle arthritis. *Foot Ankle Surg* 2020;27:809–12.
106. Munteanu SE, Landorf KB, McClelland JA, Roddy E, Cicuttini FM, Shiell A, *et al.* Shoe-stiffening inserts for first metatarsophalangeal joint osteoarthritis: a randomised trial. *Osteoarthritis Cartilage* 2021;29:480–90.
107. Paterson KL, Hinman RS, Metcalf BR, Jones SE, Menz HB, Munteanu SE, *et al.* Foot orthoses for first metatarsophalangeal joint osteoarthritis: study protocol for the FORT randomised controlled trial. *BMC Musculoskelet Disord* 2020;21:830.
108. Qi Y, Ma Y, Chen Z. Effects of ankle joint injection combined with massotherapy on function recovery and quality of life of ankle joint osteoarthrosis patients. *Int J Clin Exp Med* 2018;11:12547–54.
109. Anzolin AP, Collares DDS, Tadeu Dos Santos R, Pasqualotti A, Rossato-Grando LG, Bertol CD. Effectiveness of topical ozonated oil in severe osteoarthritis: a randomised, triple-blinded, placebo-controlled study. *Compl Ther Clin Pract* 2021;43:101351.
110. Cohen MM, Altman RD, Hollstrom R, Hollstrom C, Sun C, Gipson B. Safety and efficacy of intra-articular sodium hyaluronate (Hyalgan) in a randomized, double-blind study for osteoarthritis of the ankle. *Foot Ankle Int* 2008;29:657–63.
111. Salk RS, Chang TJ, D'Costa WF, Soomekh DJ, Grogan KA. Sodium hyaluronate in the treatment of osteoarthritis of the ankle: a controlled, randomized, double-blind pilot study. *J Bone Joint Surg Am* 2006;88:295–302.
112. Karatosun V, Unver B, Ozden A, Ozay Z, Gunal I. Intra-articular hyaluronic acid compared to exercise therapy in osteoarthritis of the ankle. A prospective randomized trial with long-term follow-up. *Clin Exp Rheumatol* 2008;26:288–94.
113. Gibson JNA, Thomson CE. Arthrodesis or total replacement arthroplasty for hallux rigidus. A randomized controlled trial. *Foot Ankle Int* 2005;26:680–90.
114. Stone OD, Ray R, Thomson CE, Gibson JN. Long-Term follow-up of arthrodesis vs total joint arthroplasty for hallux rigidus. *Foot Ankle Int* 2017;38:375–80.
115. Norvell DC, Ledoux WR, Shofer JB, Hansen ST, Davitt J, Anderson JG, *et al.* Effectiveness and safety of ankle arthrodesis versus arthroplasty: a prospective multicenter study. *J Bone Joint Surg Am* 2019;101:1485–94.
116. Wood PL, Sutton C, Mishra V, Suneja R. A randomised, controlled trial of two mobile-bearing total ankle replacements. *J Bone Joint Surg Br* 2009;91:69–74.
117. Nunley JA, Adams SB, Easley ME, DeOrio JK. Prospective randomized trial comparing mobile-bearing and fixed-bearing total ankle replacement. *Foot Ankle Int* 2019;40:1239–48.
118. Saltzman CL, Hillis SL, Stolley MP, Anderson DD, Amendola A. Motion versus fixed distraction of the joint in the treatment of ankle osteoarthritis: a prospective randomized controlled trial. *J Bone Joint Surg Am* 2012;94:961–70.
119. Conaghan PG, Kloppenburg M, Schett G, Bijlsma JW. Osteoarthritis research priorities: a report from a EULAR ad hoc expert committee. *Ann Rheum Dis* 2014;73:1442–5.
120. Crowe S, Fenton M, Hall M, Cowan K, Chalmers I. Patients', clinicians' and the research communities' priorities for treatment research: there is an important mismatch. *Res Involv Engagem* 2015;1:2.