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

Group author: International Foot and Ankle Osteoarthritis Consortium

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## 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.

*Design:* 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.

Key words: osteoarthritis, foot, consensus, review

## 1. Background

Foot and ankle osteoarthritis (OA) is common and disabling but has received less research attention than OA at other sites1, 2. To 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 (IFAOC) 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.

## 2. 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 systematic3-6 and narrative reviews1, 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 IFAOC 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 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.

## 3. Results

Thirty-one (69%) delegates from seven countries responded to the online survey. Characteristics of the respondents are provided in Table 1. Mean (SD) scores for each research agenda item are shown in Table 2. 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.

### 3.1. Definition and diagnosis

Imaging diagnosis

Traditionally, radiographic diagnosis of OA adopts the Kellgren and Lawrence (KL) system12,which was developed for knee OA13, 14. To assess the foot, an Atlas was developed to diagnose radiographic OA of the first metatarsophalangeal (MTP) joint, first cuneiform-metatarsal joint, second cuneiform-metatarsal joint, talonavicular joint, and navicular-first cuneiform joint15. The overall score has demonstrated moderate-to-excellent reliability15.

Ankle joint images have recently been incorporated into the Foot Atlas6, and a separate bespoke atlas has been developed for the ankle and rearfoot16. Intra-rater reliability for most features was good-to-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 semiquantitative MRI scoring system for the first MTP joint demonstrated excellent intra-rater and inter-rater reproducibility17, 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 in the foot and ankle, 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.

In the foot, clinical diagnostic criteria are scarce. One previous study developed a clinical diagnostic rule for identifying radiographic first MTP joint OA29with 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 pain.30 Diagnosis of midfoot OA remains reliant on location, palpation or provocation of the suspected joint in conjunction with diagnostic imaging, most commonly plain radiographs. Whilst some provocation tests assess the integrity of the midfoot joints following Lisfranc injury32, 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 and use of local anaesthesia31 has been described, however the 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

### 3.2. 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 3).

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 cuneometarsal 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 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 joints27, 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 srOA6, 27, 38, 44, 48, 50. Obesity was associated with presence of foot, first MTP joint and polyarticular foot rOA and midfoot srOA38, 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 hypermobility6, 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

### 3.3. Burden

Symptoms and impairments

Foot OA is an important contributor to the burden of OA and has a significant impact on mobility27, 44.

First MTP joint OA is associated with decreased range of first MTP joint dorsiflexion55 and increased plantar pressure under the hallux and lesser toes56-58 and altered gait patterns5960, 61.. 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 relates to significant impairment of daily activity11reduced 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 severity43, 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=53315, n=20512, n=52513).

Ankle OA is common and presents a significant burden, with ankle pain accounting for 10% of musculoskeletal-related consultations in UK primary care65. 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 pressure69-73. Those with asymmetric or unilateral ankle OA demonstrate atrophy and reduced activation of lower leg muscles74-77.

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. pThis shows poor quality of life is influenced more by symptoms than radiographic disease79.

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.

### 3.4. 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 pain84-86, the FHSQ pain domain87-89, the Manchester Foot Pain and Disability Index function subscale 86, 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, FFI-RS pain subscale and 100mm VAS of walking pain severity in individuals with first MTP joint OA95, and acceptable responsiveness has been reported for the AOFAS, SEFAS and FAOS in individuals undergoing surgery for ankle OA96-98. 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 strength84, 87, kinetics86, 87 and kinematics84, 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 valid94, 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

### 3.5. 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 pain104, 105, but no RCTs have investigated the effectiveness of weight loss interventions for foot and ankle OA.

Devices including footwear, ankle orthoses and foot orthoses

Two RCTs88, 106 have investigated the efficacy of footwear and foot orthoses for first MTP joint OA. Menz et al88 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 al89 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 a sham flat insole 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 onto 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®111, unbranded112 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 trials111 112 used multiple dosing regimens (1 ml weekly injection for 5 weeks), whereas one91 used a single dose.Two head-to-head RCTs. Karatosun et al113 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 two114 and 15 years115 in individuals with first MTP joint OA showed a significant between-group difference in pain favouring arthrodesis at two and 15 years. Baumhauer et al85 compared hemi-arthroplasty (Cartiva®) to arthrodesis for first MTP joint OA in a non-inferiority trial. There was a significant difference between groups in favour of arthrodesis for pain and function at two years.

For ankle OA, the main surgical options are fusion. and total ankle replacement. In one trial, Norvell et al116 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.. Wood et al117, 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 al118 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 al119 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

## 4. 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 osteoarthritis (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.120, 121 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 our approach 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 ranking 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.

### Competing interests

 None of the authors has a competing interest to declare.

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### Table 1. Characteristics of delegates who completed the scoring of research agenda items (n=31).

|  |  |
| --- | --- |
| 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 2. Mean (SD) scores for each research agenda item from the symposium delegates (n=31). Shaded items met the prespecified criteria of ≥70.

|  |  |  |
| --- | --- | --- |
|  | 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) |
| 14. Quantify the economic and societal burden of foot and ankle OA | 85.3 (16.7) |
| Outcome assessment | 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) |
| 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) |
| Treatment | 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 3. Characteristics of key epidemiology studies reporting prevalence and incidence of foot and ankle OA.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 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 APWB 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 APWB 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: cuneometatatarsal; NC: navicular-first cuneiform; TN: talonavicular; WB: weightbearing; AP: antero-posterior; OP: osteophytes; JSN: joint space narrowing |