



## 17 **Abstract**

18 **Objectives:** To identify by systematic review published prevalence estimates of radiographic ankle  
19 osteoarthritis (OA) and to subsequently estimate the prevalence of ankle pain and symptomatic,  
20 radiographic ankle OA within community-dwelling older adults from North Staffordshire, UK.

21 **Methods:** Electronic databases were searched using terms for ankle, osteoarthritis and radiography. Data  
22 regarding population, radiographic methods, definitions and prevalence estimates of ankle OA were  
23 extracted from papers meeting predetermined selection criteria. Adults aged  $\geq 50$  years and registered with  
24 four general practices in North Staffordshire were mailed a health questionnaire. Ankle pain in the previous  
25 month was determined using a foot and ankle pain manikin. Respondents reporting pain in or around the  
26 foot in the last 12 months were invited to attend a research clinic where weight-bearing, antero-posterior  
27 and lateral ankle radiographs were obtained and scored for OA using a standardised atlas. Prevalence  
28 estimates for ankle pain and symptomatic, radiographic ankle OA were calculated using multiple  
29 imputation and weighted logistic regression, and stratified by age, gender and socioeconomic status.

30 **Results:** Eighteen studies were included in the systematic review. The methods of radiographic  
31 classification of ankle OA were poorly reported and showed heterogeneity. No true general population  
32 prevalence estimates of radiographic ankle OA were found, estimates in select sporting and medical  
33 community-dwelling populations ranged from 0.0-97.1%. 5109 participants responded to the health survey  
34 questionnaire (adjusted response 56%). Radiographs were obtained in 557 participants. The prevalence of  
35 ankle pain was 11.7% (10.8,12.6) and symptomatic, radiographic ankle OA grade $\geq 2$  was 3.4% (2.3, 4.5)  
36 (grade $\geq 1$ : 8.8% (7.9,9.8); grade=3: 1.9% (1.0,2.7). Prevalence was higher in females, younger adults (50-64  
37 years) and those with routine/manual occupations.

38 **Conclusion:** No general population prevalence estimates of radiographic ankle OA were identified in the  
39 published literature. Our prevalence study found that ankle pain was common in community-dwelling older  
40 adults, whereas moderate to severe symptomatic, radiographic ankle OA occurred less frequently. Further  
41 investigations of the prevalence of ankle OA using more sensitive imaging modalities are warranted.

42

## 43 **Introduction**

44 Osteoarthritis (OA) is a recognised global burden of disease, affecting more than 100 million people  
45 worldwide [1]. The prevalence of symptomatic, radiographic OA in adults aged 60 years and over is  
46 reported to be 10% for men and 18% for women, and as populations age, it is predicted that OA will  
47 become one of the leading causes of disability worldwide by the year 2020 [2]. OA at joint sites such as the  
48 knee, hip and hand have received considerable attention, in comparison, the foot and ankle joints have  
49 been relatively neglected. The prevalence of ankle OA within the general population is not clear, but clinical  
50 observations and experience suggest that it is significantly lower than OA of the knee or hip [3]. Estimates  
51 of the prevalence of ankle pain range from 9% to 15% in general adult populations [4,5].

52  
53 Previous reviews have examined the methods of radiographic assessment at the knee, hip, hand and foot  
54 [6, 7, 8, 9]. However, the methods used to examine radiographic ankle OA and define its presence have not  
55 been reviewed previously, and estimates of ankle OA have ranged widely between 0 and 97% [10,11]. The  
56 variations between studies regarding the methods and definitions used for radiographic ankle OA, as well  
57 as the characteristics of the study populations examined, may explain the differences in reported  
58 prevalence estimates between studies.

59  
60 While the population prevalence of ankle pain within the general population has been estimated previously  
61 [4, 5, 12, 13], there seems to be a paucity of existing studies examining radiographic ankle OA in  
62 community-dwelling populations. Population prevalence estimates for both ankle pain and symptomatic,  
63 radiographic ankle OA would demonstrate the burden of these two conditions within a community setting  
64 more clearly and inform healthcare provision and clinical needs. It would also provide a basis for  
65 understanding better the aetiology of ankle OA and the association between ankle pain and the occurrence  
66 of OA.

67

68 The objective of this study was (i) to undertake a systematic review to identify existing prevalence  
69 estimates for radiographic ankle OA in community-dwelling populations and (ii) to estimate the prevalence  
70 of ankle pain and symptomatic radiographic ankle OA in a population of community-dwelling older adults  
71 aged 50 years and over.

72

## 73 **Materials and Methods: Systematic Review**

### 74 **Search strategy**

75 A search strategy was developed in order to identify all community-dwelling epidemiological studies which  
76 examined radiographic ankle OA in adults. Electronic searches were conducted in Medline, Embase and  
77 CINAHL and all studies registered on these databases from inception until the search date (31<sup>st</sup> December  
78 2016) were eligible for inclusion in this review. The search strategy used the subject index terms  
79 'osteoarthritis', 'radiology' 'radiography', 'x-ray', 'x-ray film' and 'ankle' as well as the following free text  
80 terms: osteoarthr\* or degenerative arthr\* or OA AND radiograph\* or radiolog\* or x ray or imaging or  
81 rontgen\* or roentgen\* AND ankle or ankle joint or talus or talar or talocrural or talotibial or talofibul\* or  
82 tibiotal\* or tibiofibul\* or hindfoot or hind foot). This review was conducted and reported in line with the  
83 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (S1 File).

84

### 85 **Search criteria**

86 A single reviewer (CM) screened the titles and abstracts using the following selection criteria. The inclusion  
87 criteria were: (1) human subjects, (2) the study population contained adults aged 18 years and over, (3)  
88 plain film radiography was used to assess the presence of ankle OA, (4) the study population was from a  
89 community-dwelling or population. Exclusion criteria were: (1) non-human studies, (2) studies that involved  
90 solely children (<18 years), (3) studies that used only macro radiography, computerised tomography,  
91 magnetic resonance imaging, ultrasound or scintigraphy, (4) studies that recruited patients from secondary  
92 or tertiary care settings, (5) clinical trials or narrative reviews, (6) incomplete or un-published articles.

93

## 94 **Data extraction and synthesis**

95 Titles and abstracts not excluded or those whose relevance was ambiguous were retained for full-text  
96 review. A single reviewer (CM) assessed the full texts and conferred with two other researchers (ER, MM)  
97 when uncertainty remained. Two non-English articles were identified in the search and translations were  
98 obtained. Additionally, reference lists of papers included in the review were also screened for further  
99 relevant articles.

100

101 Data extracted from all papers that satisfied the selection criteria included the following information: study  
102 population and demographics, anatomical definition of the ankle joint, radiographic views, method of  
103 radiographic assessment of ankle OA including reliability, definition of radiographic ankle OA and  
104 prevalence estimates of radiographic ankle OA. Quality assessment was performed using the 8-item  
105 Newcastle-Ottawa Quality Appraisal Scale, by a single reviewer (CM) who conferred with two other  
106 researchers (ER, MM) when uncertainty remained [14]. The scale was modified to 5-items for cross-  
107 sectional studies questions by dropping questions related to longitudinal study design.

108

## 109 **Results: Systematic Review**

### 110 **Search**

111 The search identified 1517 unique papers of which 1446 were excluded through review of titles and  
112 abstracts (Fig 1). After full-text review of the remaining 71 publications, a further 57 were excluded, leaving  
113 14 papers to be included. Screening the reference lists of these papers identified a further four studies  
114 suitable for inclusion. Therefore, a total of 18 papers were included [10,11,15-30].

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117 **Fig 1. Flow diagram of publications included and excluded at each stage of the review**

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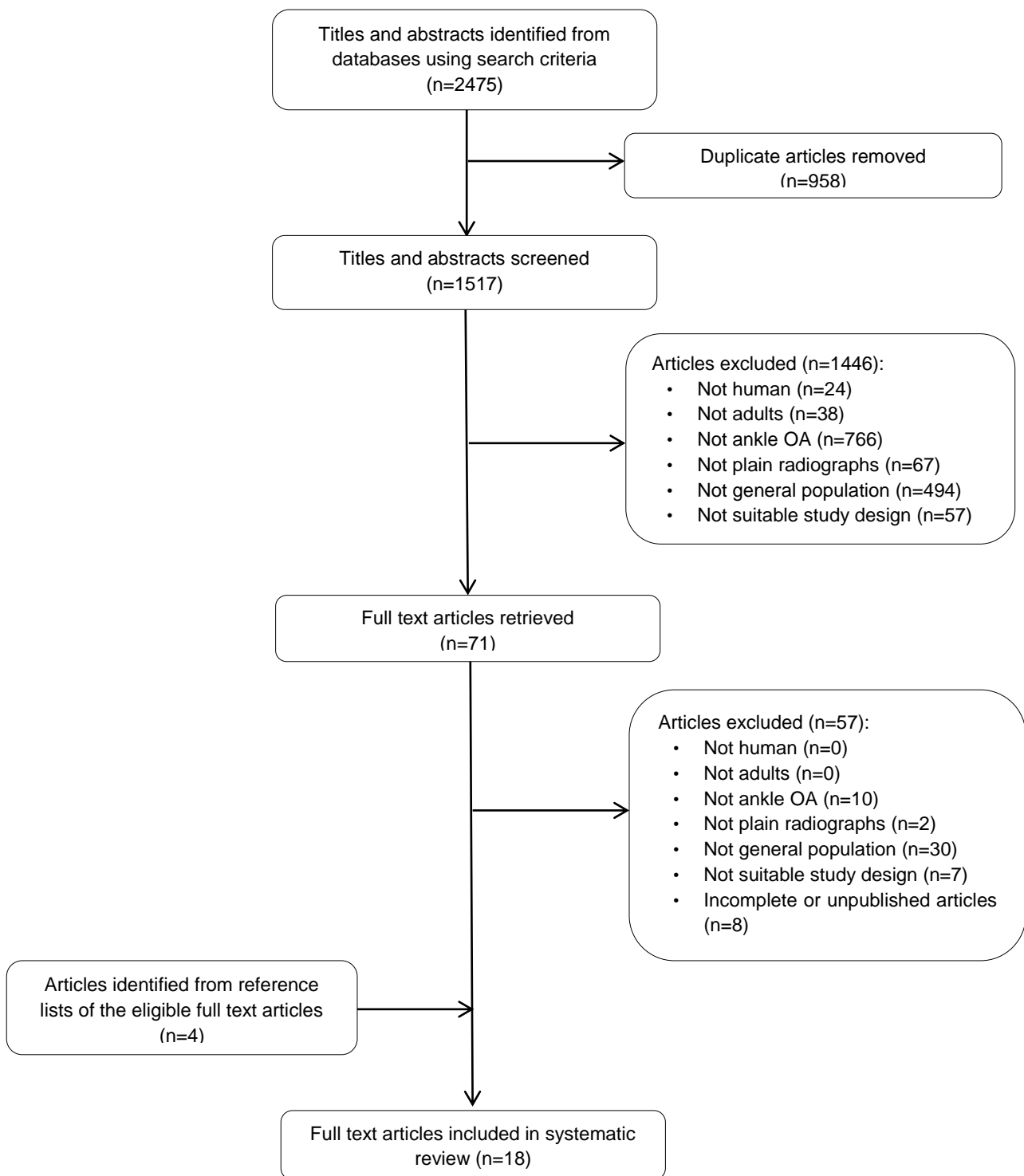
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## 132 **Quality appraisal**

133 Quality appraisal using the Modified Newcastle Ottawa Scale Score demonstrated that no studies were of  
134 exceptionally high quality (Table 1). All studies assessed ankle OA radiographically however, the majority of  
135 studies were limited by being undertaken in populations selected specific from sporting groups or with a  
136 particular medical condition (n=15) [10,11,15-26,30].

137

## 138 **Study population**

139 Sample sizes were frequently small: nine studies had  $\leq 50$  participants [10,16-21,23,28], three studies had  
140 51-100 [22,24,29] and six studies had  $>100$  [11,15,25-27,30]. The study populations were frequently  
141 specific sub-groups within a community setting rather than representing true general populations (Table 1).  
142 No study reported general population prevalence estimates for radiographic ankle OA. Fifteen studies used  
143 select sporting populations [10,11,15-26,30], one used a population with hereditary haemochromatosis  
144 [27], one utilised human cadavers [28] and one involved a small urban population in Nigeria who were  
145 attending a primary care facility with joint symptoms [29]. All studies included adults although these were  
146 frequently younger adults: in two studies age range was not reported but mean age was 35 years [18] and  
147 50 years [30], six studies reported age range with an upper limit of 55 years [11,15,19,21,24,26], ten studies  
148 showed an age range which extended past 55 years [10,16,17,20,22,23,25,27-29]. Nine studies examined  
149 exclusively male populations [10,15-18,21,22,26,30] and one study examined an exclusively female  
150 population [20]. One study did not report the gender of their population [24].

151

## 152 **Joints examined and radiographic views**

153 Most studies broadly described studying the 'ankle joint' while five specifically described the exact regions  
154 of the ankle that were examined radiographically for OA and variations were present between these  
155 studies (Table 1) [11,17,24,25,28]. Eight studies failed to provide details of the radiographic views that were  
156 used to assess ankle OA [11,17,19,20,26,28-30]. The remaining ten all included an anterior-posterior view  
157 with six also obtaining a lateral view [10,15,16,18,21-25,27]. Seven studies provided information regarding

158 whether views were weight-bearing [15,18,21-24,30]. The radiographic assessment technique was not  
159 described in three studies [11,28,29].

160

161 Ten studies graded individual radiographic features to assess the presence of OA [10,15,18-20,22-26]: nine  
162 of these studies graded osteophytes [10,15,18-20,22,24-26], seven joint space narrowing/width [15,18-  
163 20,23-25] and five subchondral sclerosis [15,18-20,26]. The six remaining studies used established grading  
164 systems: the Kellgren and Lawrence scoring system (0-4) [27,30,31], the Scranton and McDermott Score (I-  
165 IV) [16,17,32], the modified Hermodsson Scale [20], and the unmodified [16,17,33] and modified [21]  
166 Bargon Arthrosis Score (Table 1). None of the studies that assessed radiographic ankle OA included  
167 symptoms in their definitions of ankle OA. Reliability of the radiographic assessment of ankle OA was  
168 assessed and reported in only two studies [16,17].



**Table 1. Description of the populations and the radiographic assessment undertaken in publications included in the review**

Study	Population	Newcastle Ottawa Scale score†	Sample size	Age range in years (mean)	% Female	Joints examined	Radiographic views	Radiographic assessment	Reliability	Ankle OA definition	Prevalence estimate of ankle OA
Adams, 1979 [24]	Football club; Leeds, UK	1/5	62	15-55 (23)	NR	Tibia and talar surfaces	NWB, AP & LAT	IRF (P/A): OST, JSN, LB, NBF	NR	Presence of JSN & NBF	1.6%
Andersson et al., 1989 [23]	Retired ballet dancers; Sweden; Norway; Copenhagen, Denmark	1/5	44	44-80 (57)	66%	Ankle	NWB, AP & LAT	IRF (P/A): JSN	NR	Presence of obvious JSN	2.3%
Armenis et al, 2011 [15]	Former elite football players aged >40 years & gender matched non-sporting controls; Athens, Greece	2/5	182	42-55 (50)	0%	Ankle	WB, AP	IRF (P/A): OST, JSN, SCL, CYT	NR	NR	Former football players: 8.8%, Control population: 3.7%
Brodelius, 1961 [11]	Football players, ballet dancers & patients examined with a foot injury; Malmo, Sweden	1/5	245	18-46 (NR)	35%	Talar joints	NR, NR	NR	NR	NR	Football players: 97.1%, Ballet dancers: 87.5%, Control patients: <24 years 3.0% & >45 years 50.0%
Carroll et al., 2011 [27]	Individuals from general population ≥40 years with hereditary haemochromatosis; Western Australia	1/5	103	41-83 (NA)	58%	Ankle	NR, AP & LAT	Kellgren & Lawrence score	NR	Grade ≥2 in both ankles	1.9%
Gross & Marti, 1999 [18]	Former league volleyball players & normal healthy gender matched controls; Magglingen, Sweden	2/5	41	NR (35)	0%	Ankle	WB, AP	IRF: OST (0-3), JSN (0-3), SCL talar & tibial (0-3)	NR	Sum score for IRF >2	Volleyball players: 86.4%, Untrained males: 22.2%
Iosifidis et al., 2015 [30]	Former elite male athletes and controls; Greece	2/5	335	NR (50)	0%	Ankle	WB, NR	Kellgren & Lawrence score	NR	Grade ≥2	Former athletes: 7.0%, Controls: 3.7%
Jenyo et al., 2014 [29]	Primary care patients with joint symptoms; Osun State, Nigeria	2/5	90	20-60 (NR)	60%	Ankle	NR, NR	NR	NR	NR	NR
Knobloch	Former national team long	6/9	50	33-46 (39)	0%	Ankle	WB, AP	Bargon	NR	Grade ≥3	Runners &

et al., 1990 [21]	distance runners, orienteers, bobsledders & healthy individuals matched by gender recruited from a previous RCT; Switzerland							arthrosis score (modified; 0-4)			orienteers: 59.3%, Bobsledders: 44.4%, Healthy individuals: 26.3%
Konradsen et al., 1990 [22]	National orienteers & non-running patients referred for abdominal radiology exams matched for age, weight, height and physical work load; Denmark	3/5	54	50-68 (58)	0%	Ankle	WB, AP & LAT	IRF (P/A): OST, Cartilage thickness (mm)	NR	Cartilage thickness ≤3mm	NR
Muehlema n et al., 1997 [28]	Cadavers; Chicago, USA	2/5	50	36-94 (76)	52%	Talocrural	NR, NR	NR	NR	NR	NR
Murray-Leslie et al., 1977 [25]	Ex-military and sport parachutists; Leeds, UK	1/5	221	23-70 (38)	5%	Talotibial	NR, AP	IRF: OST (0-4), JSN (0-4)	NR	Grade >2 for OST or JSN	17.5%
Panush et al., 1986 [10]	Runners aged >50 years weekly distance ≥32km (20 miles) for ≥5 years & non-runners with normal body weight; Florida, USA	2/5	35	50-74 (59)	0%	Ankle	NR, AP & LAT	IRF (P/A): OST, Cartilage thickness (mm)	NR	Cartilage thickness ≤3mm	Runners: 0.0%, Non-runners: 0.0%
Schmitt et al., 2003 [17]	Former male high jump athletes & age & BMI matched male controls; Heidelberg, Germany	3/5	40	32-56 (42)	0%	Talotibio fibular	NR, NR	Bargon arthrosis score (0-3), Scranton & McDermott score (I-IV)	Inter-rater: K=0.57-1.00, Intra-rater: NR	NR	NR
Schmitt et al., 2004 [16]	Former long and triple jump athletes; Germany	3/9	29	36-59 (44)	0%	Ankle	NR, AP & LAT	Bargon arthrosis score (0-3), Scranton & McDermott score (I-IV)	Inter-rater: K=0.57, Intra-rater: K=1.00	Bargon score ≥1, Scranton & McDermott score ≥2	Bargon score: Push-off leg = 75.0%, Swing leg = 67.9%; Scranton & McDermott score: Push-off leg = 39.3%, Swing leg = 39.3%
Teitz & Kilcoyne, 1998 [19]	Former professional dancers for >10 years & age matched non-dancers with lower limb injuries or pain;	2/5	50	27-46 (35)	64%	Ankle	NR, NR	IRF (P/A): OST, JSN, SCL, CYT	NR	NR	Professional dancers: 50.0%, Non-dancers: 0.0%

	Washington, USA										
Van Dijk et al., 1995 [20]	Former professional dancers aged 50-70 years & gender, age, height & weight matched outpatients with no lower limb complaints; Amsterdam, Netherlands	3/5	38	50-66 (59)	100%	Ankle	NR, NR	IRF (P/A): OST, SCL, CYT, BD, JSW (mm), Hermodsson scale (modified, 0-3)	NR	NR	NR
Vincelette et al., 1972 [26]	Football players & unspecified gender matched control population; Montreal, Canada	3/5	109	19-30 (23)	0%	Ankle	NR, NR	IRF (P/A): OST, SCL, Irregular joint line	NR	Mild OA = 1 IRF, Severe OA = 2-3 IRFs	Football players: mild = 30.0%, severe = 63.0%; Controls: mild = 6.0%, severe = 0.0%

† The Newcastle-Ottawa quality assessment scale was marked out of nine for cohort studies (with 1 item contributing 2 points) and modified and marked out of five for cross-sectional studies with higher scores indicating more rigorous methodological design. OA: Osteoarthritis; NR: Not reported; NA: Not applicable; WB: Weight-bearing; NWB: Non weight-bearing; AP: Anterior-Posterior View; LAT: Lateral View; IRF: Individual Radiographic Features; P/A: Presence/absence; OST: Osteophytes; JSN: Joint Space Narrowing; LB: Loose Bodies; NBF: New Bone Formation; SCL: Sclerosis; CYT: Cysts; JSW: Joint Space Width; BD: Bone Destruction; K: Kappa.

## 169 **Prevalence estimates of radiographic ankle OA**

170 Thirteen publications reported prevalence estimates for radiographic ankle OA ranging from 0.0%  
171 populations of runners, non-runners and those with reported lower limb injuries or pain [19,10] to 97.1% in  
172 a population of football players [11] however, none of these were representative of a general population  
173 (Table 1) [10,11,15,16,18,19,21,23-27,30]. Eight publications presented comparison estimates between  
174 select populations and a control group, with higher estimates for the selected population compared to the  
175 control group in each study [10,11,15,18,,19,21,25,30]. In only one study were the prevalence estimates for  
176 radiographic ankle OA stratified by age and then only for the control group [11]. As a result of this, it was  
177 not possible to undertake a meta-analysis to calculate a pooled prevalence estimate.

178

## 179 **Materials and Methods: Prevalence Study**

### 180 **Study design and data collection**

181 This study used baseline cross-sectional data collected from a prospective population-based cohort study,  
182 the Clinical Assessment Study of the Foot (CASF) [34,35]. A total of 9194 adults aged 50 years and over  
183 registered with four general practices in North Staffordshire, UK, irrespective of consultation for foot or  
184 ankle problems, were mailed a baseline health survey questionnaire which collected the following  
185 information: demographic, socioeconomic, general health, anthropometric measurements, Short Form 12  
186 (SF-12) [36], Hospital Anxiety and Depression Scale (HADS) [37], details of foot and ankle pain including  
187 duration of foot pain in the last one year, the Manchester Foot Pain and Disability Index (MFPDI) pain and  
188 functional limitation subscales [38] and a foot pain manikin asking areas of pain in the past one month to  
189 be shaded (©The University of Manchester 2000. All rights reserved.) [39]. All participants provided written  
190 informed consent and ethical approval was obtained from the Coventry Research Ethics Committee, UK  
191 (REC reference number: 10/H1210/5).

192

193 Participants who reported experiencing pain in or around the foot within the last 12 months and who  
194 consented to further contact were invited to attend a research clinic for further clinical assessment and  
195 radiographic imaging [34]. At the research clinic, weight-bearing, antero-posterior radiographs of both  
196 ankle joints and lateral views of both feet were obtained according to a standardised protocol [34].  
197

198 Radiographic grading of ankle OA assessed the articulation between the talus, tibia and fibula. A single blind  
199 assessor used a standardised atlas (developed as an extension of one recently developed for the foot, due  
200 to the lack of an appropriate scoring system for assessing individual radiographic features in ankle OA at  
201 the time) [40], where the presence of osteophytes and joint space narrowing were graded on a scale of 0-3  
202 in both views. The presence of osteophytes at the ankle joint was graded as absent (score = 0), small (score  
203 = 1), moderate (score = 2) or severe (score = 3), and presence of joint space narrowing was graded as none  
204 (score = 0), definite (score = 1), severe (score = 2), or joint fusion at one point or more (score = 3).

205 Radiographic images for the standardised classification atlas were assessed by three of the authors  
206 (radiographer MM, rheumatologist ER and podiatrist HBM) for possible representativeness of each grade  
207 (0-3) for osteophytes and joint space narrowing from which a provisional atlas was compiled. This  
208 provisional atlas was reviewed by the development team (MM, ER and HBM) and where an image was  
209 deemed unsuitable due to the presence of other OA features or imprecise patient positioning, it was  
210 replaced with another that was considered to be a better representation. This process was repeated until  
211 there was consensus amongst the team for every image representing each of the grades (0-3) for both of  
212 the OA features. In order to confirm quality and clinical relevance, the collection of images for inclusion in  
213 the ankle atlas were then reviewed by a specialist consultant musculoskeletal radiologist (Dr J Saklatavala)  
214 before the Radiographic Classification Atlas of Ankle Osteoarthritis was finalised (S2 File).

215  
216 Radiographic ankle OA was defined as a grade  $\geq 2$  for either osteophyte or joint space narrowing on either  
217 view. Intra-rater reliability of the presence of ankle OA was examined by the assessor (MM) rescoring 60  
218 randomly selected radiographs after a period of at least 8 weeks. Inter-rater reliability was examined by a  
219 second blind assessor (HBM) scoring the same 60 randomly selected radiographs. Intra-rater reliability for

220 the presence of ankle OA was shown to be excellent ( $\kappa = 0.87$ , 95% exact agreement) and inter-rater  
221 reliability was found to be fair ( $\kappa = 0.30$ , 65% exact agreement). An independent third blind assessor  
222 (CB) was subsequently asked to score the radiographs and inter-rater reliability remained low with both  
223 MM ( $\kappa = 0.18$ , 60% exact agreement) and HBM ( $\kappa = 0.30$ , 65% exact agreement).

224

## 225 **Case definitions and exclusions**

226 Ankle pain was defined as pain in the past month indicated by shading of the ankle area on the dorsal view  
227 of a foot pain manikin [39]. Symptomatic radiographic ankle OA was defined as the presence of ankle pain  
228 and radiographic ankle OA (grade $\geq$ 2 for either osteophytes or joint space narrowing on either view) in the  
229 same ankle.

230

231 Participants with a history of inflammatory arthritis (rheumatoid arthritis, psoriatic arthritis or non-specific  
232 inflammatory arthritis) identified in their medical records (primary care or local hospital) or in the clinical x-  
233 ray report by a consultant musculoskeletal radiologist were excluded from the analyses.

234

## 235 **Statistical analysis**

236 To estimate the prevalence of ankle pain and symptomatic radiographic ankle OA, multiple imputation  
237 combined with weighted logistic regression modelling was used. Analysis of the CASF study has previously  
238 shown that while responders to the baseline health survey questionnaire were broadly representative of  
239 the baseline eligible population, there was selective non-participation in the research clinics [35]. Older  
240 women (aged 75 years and over) were under-represented whilst those who attended higher education,  
241 were of a professional or managerial occupational class, had a higher number of days with foot pain and  
242 greater functional impairment on the MFPDI were more likely to attend the research clinics. Multiple  
243 imputation was used to impute missing data that arose from non-completion of individual items or  
244 questionnaire non-response. Missing data were associated with a number of variables and therefore data  
245 were assumed to be missing at random. The imputation model included the following variables, which

246 included those associated with missing data: age, gender, GP practice, marital status, higher education,  
247 employment status, socioeconomic class, SF-12 score, HADS score, reported foot pain in last month,  
248 duration of foot pain in last 12 months and Rasch-transformed MFPDI pain and function scores. The MFPDI  
249 has previously been shown to fit the Rasch model, allowing interval-level scores to be generated for the  
250 pain and function subscales from the instrument that has ordinal responses, so that severity of pain and  
251 disability can be more precisely described [41]. The number of imputations was set at 15 and the imputed  
252 datasets were combined using Rubin's rules [42]. The `mim:proportion` command was used to determine  
253 the prevalence estimates and 95% confidence intervals for all responders to the baseline health survey  
254 questionnaire.

255

256 Prevalence estimates were then weighted to account for any differences in age, gender and GP practice  
257 between responders and non-responders to the questionnaire. Logistic regression modelled for each  
258 person the probability of completing the questionnaire based on their age, gender and general practice.  
259 The inverse of the probability was used to obtain weighted prevalence estimates (and 95% confidence  
260 intervals) in the total baseline eligible mailed population from North Staffordshire. Population prevalence  
261 estimates for ankle pain and symptomatic radiographic foot OA were stratified for age, gender and  
262 socioeconomic status. Sensitivity analysis using different severity thresholds of radiographic OA that  
263 included  $\text{grade} \geq 1$  and  $\text{grade} = 3$  were also examined using the same processes of multiple imputation and  
264 weighted logistic regression. All analyses were undertaken using STATA version 12.0 (Stata Corporation,  
265 Texas, USA).

266

## 267 **Results: Prevalence Study**

### 268 **Study population**

269 The CASF study identified a total of 9403 adults aged 50 years and over within four GP practices in North  
270 Staffordshire however, following exclusions prior to and during mailing, a total of 9194 mailed participants  
271 were determined to be eligible. In total, there were 5109 responders to the baseline health survey

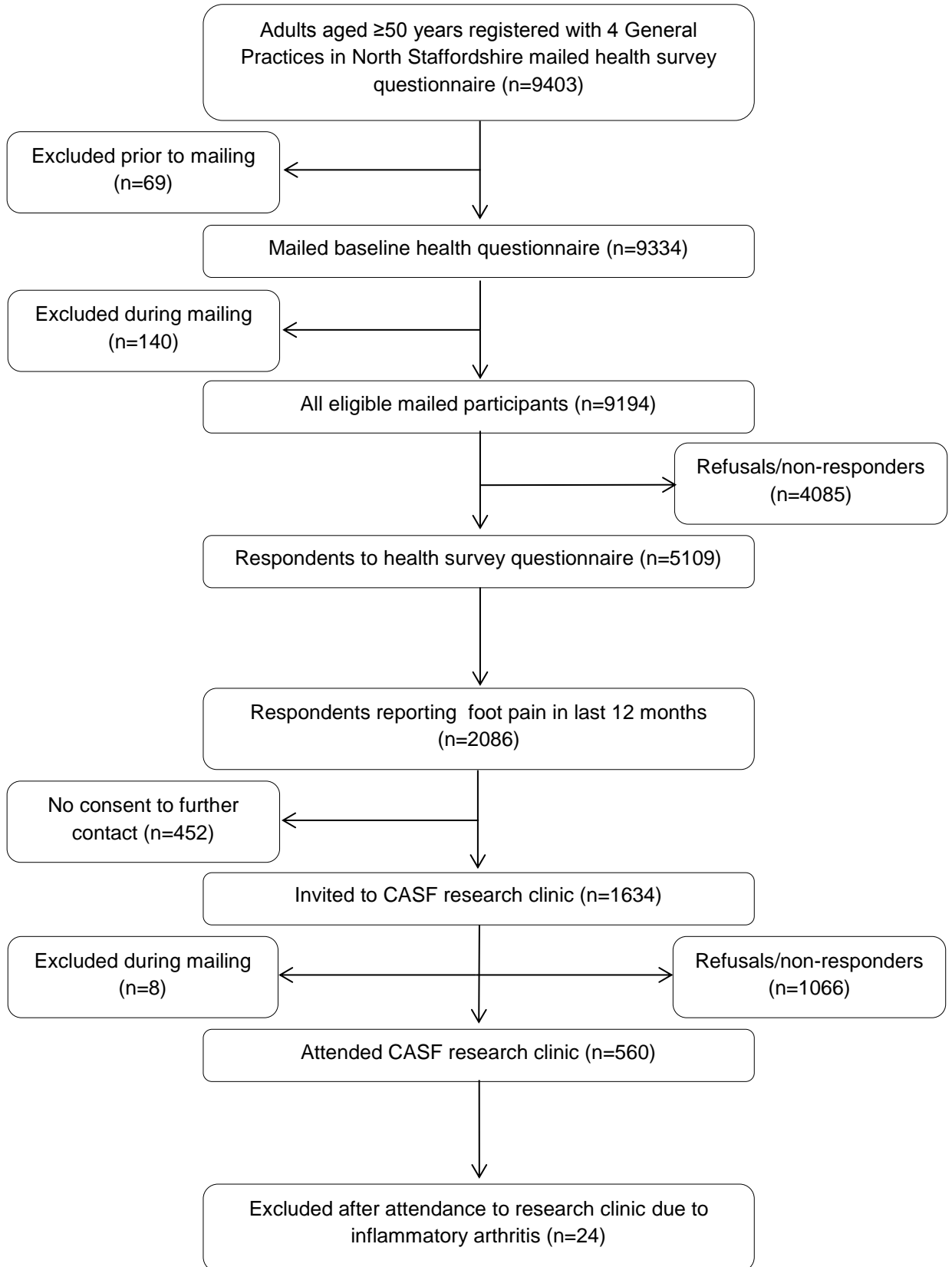
272 questionnaires (adjusted response 56%), with 2086 of these (41%) reporting pain in or around the foot in  
273 the last 12 months (Fig 2). 1634 of these provided consent to further contact and were invited to attend a  
274 research clinic. A total of 560 participants attended the research clinics (adjusted response rate 34%).  
275 Participants with inflammatory arthritis were excluded from this analysis (n=24). Of the 536 eligible  
276 individuals without inflammatory arthritis who attended the research clinic, eight had incomplete ankle  
277 pain data and four had incomplete radiographic data. Full details of the reasons for exclusion and refusals  
278 to take part have been detailed elsewhere [35]. Demographic characteristics of responders and selective  
279 non-participation have also been discussed previously [35].

280

281



282 **Fig 2. Flow diagram showing CASF study recruitment**



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## 286 **Prevalence of symptomatic radiographic ankle OA**

287 In the clinic attenders, 31.9% (n=167) had ankle pain and 7.4% (n=39) had symptomatic radiographic ankle  
288 OA. Using multiple imputation in these individuals allowed the frequency of ankle pain and symptomatic  
289 radiographic ankle OA to be determined for the responder population. This showed the prevalences of  
290 ankle pain to be 11.6% (95%CI 10.8, 12.5) and symptomatic radiographic ankle OA to be 3.3% (2.4, 4.3).

291

292 To extrapolate these results to the total eligible baseline population of community-dwelling adults aged 50  
293 years and over in North Staffordshire, weighted logistic regression was performed using the variables age,  
294 gender and general practice which were known for all individuals. The prevalence of ankle pain was 11.7%  
295 (10.8, 12.6) and symptomatic radiographic ankle OA, 3.4% (2.3, 4.5).

296

## 297 **Stratification of prevalence estimates**

298 Both ankle pain and symptomatic radiographic ankle OA were more prevalent in females and in younger  
299 individuals aged 50-64 years (Table 2). However, there was considerable overlap of the confidence intervals  
300 for the prevalence estimates for the different age groups and genders. Individuals identified as having  
301 routine or manual occupations demonstrated higher prevalence estimates of both ankle pain and  
302 symptomatic radiographic ankle OA, which remained the case after further sub-stratification by age and  
303 gender (Table 3).

304

## 305 **Sensitivity analysis of different thresholds of radiographic severity**

306 Using a lower threshold of radiographic severity of grade $\geq$ 1 for either osteophytes or joint space narrowing  
307 on either view the prevalence of symptomatic radiographic ankle OA to be 8.8% (7.9, 9.8). Whereas using a  
308 higher threshold of grade=3 for either osteophytes or joint space narrowing on either view resulted in a  
309 prevalence estimate of 1.9% (1.0, 2.7). Irrespective of the threshold used to define radiographic OA,  
310 symptomatic radiographic ankle OA was still more prevalent in females, in younger individuals aged 50-64  
311 years and in individuals identified as having routine or manual occupations (Table 4).



313 **Table 2. Population prevalence estimates of ankle pain and symptomatic radiographic ankle OA, overall**  
 314 **and stratified by age and gender.**  
 315

	<b>Proportion estimate for ankle pain: % (95% CI)</b>	<b>Proportion estimate for SR ankle OA: % (95% CI)</b>
<b>Overall</b>	11.7 (10.8, 12.6)	3.4 (2.3, 4.5)
<b>Gender:</b>		
Males	9.2 (8.0, 10.4)	2.9 (1.9, 3.9)
Females	14.1 (12.8, 15.5)	3.9 (2.3, 5.4)
<b>Age (years):</b>		
50-64	12.2 (10.9, 13.5)	3.6 (2.4, 4.8)
65-74	11.2 (9.6, 12.8)	3.2 (1.8, 4.7)
≥75	11.1 (9.1, 13.0)	3.1 (1.6, 4.6)
<b>Males by Age (years):</b>		
50-64	10.3 (8.6, 12.0)	3.4 (2.0, 4.7)
65-74	7.7 (5.8, 9.7)	2.4 (0.9, 3.9)
≥75	7.8 (5.2, 10.5)	2.3 (0.4, 4.3)
<b>Females by Age (years):</b>		
50-64	14.1 (12.2, 16.1)	3.8 (2.0, 5.6)
65-74	14.7 (12.1, 17.2)	4.1 (1.8, 6.5)
≥75	13.5 (10.7, 16.9)	3.6 (1.5, 5.8)

316 *CI: Confidence interval; SR: Symptomatic radiographic; OA: Osteoarthritis.*  
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**Table 3. Population prevalence estimates of ankle pain and symptomatic radiographic ankle OA, stratified by socioeconomic status and age and gender**

	<b>Proportion estimate for ankle pain: % (95% CI)</b>	<b>Proportion estimate for SR ankle OA: % (95% CI)</b>
<b>Socioeconomic status</b>		
Managerial & professional	7.6 (5.9, 9.3)	2.4 (1.0, 3.7)
Intermediate	10.9 (8.8, 13.0)	3.0 (1.4, 4.5)
Routine & manual	13.0 (11.7, 14.3)	4.1 (2.6, 5.6)
Other*	13.9 (10.9, 16.9)	2.5 (-0.5, 5.6)
<b>Males by socioeconomic status</b>		
Managerial & professional	5.2 (3.4, 7.1)	1.5(0.1, 2.9)
Intermediate	8.9 (6.1, 11.7)	3.1 (1.0, 5.3)
Routine/ manual	10.6 (8.8, 12.3)	3.6 (2.1, 5.2)
Other*	12.1 (7.1, 17.1)	1.9 (-1.3, 5.1)
<b>Females by socioeconomic status</b>		
Managerial & professional	10.9 (7.9, 13.9)	3.5 (1.3, 5.7)
Intermediate	12.7 (9.7, 15.8)	2.8 (0.6, 5.0)
Routine & manual	15.4 (13.5, 17.3)	4.5 (2.4, 6.6)
Other*	14.8 (11.0, 18.5)	3.0 (-0.6, 6.6)
<b>Age 50-64 years by socioeconomic status</b>		
Managerial & professional	7.7 (5.4, 10.0)	2.5 (0.8, 4.2)
Intermediate	10.5 (7.7, 13.3)	2.7 (0.9, 4.6)
Routine & manual	13.6 (11.7, 15.4)	4.3 (2.6, 6.1)
Other*	17.9 (12.7, 23.1)	3.6 (-1.1, 8.2)
<b>Age 65-74 years by socioeconomic status</b>		
Managerial & professional	7.7 (4.6, 10.8)	2.3 (-0.2, 4.9)
Intermediate	10.0 (6.2, 13.8)	2.7 (0.1, 5.4)
Routine & manual	12.1 (9.9, 14.4)	3.8 (1.8, 5.7)
Other*	14.1 (8.6, 19.6)	2.7 (-1.7, 7.2)
<b>Age ≥75 years by socioeconomic status</b>		
Managerial & professional	7.0 (3.1, 10.8)	2.0 (-0.5, 4.5)
Intermediate	13.6 (8.5-18.8)	4.0 (0.3, 7.8)
Routine & manual	12.8 (9.8, 15.7)	3.9 (1.3, 6.4)
Other*	7.1 (3.2, 11.1)	0.8 (-0.7, 2.3)

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\* The 'other' category includes housewives and individuals whose occupational class could not be determined or was inadequately described. CI: Confidence interval; SR: Symptomatic radiographic; OA: Osteoarthritis.

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**Table 4. Population prevalence estimates of symptomatic radiographic ankle OA using different grade of radiographic severity, stratified by socioeconomic status and age and gender**

	Proportion estimate for SR ankle OA (grade≥1): % (95% CI)	Proportion estimate for SR ankle OA (grade=3): % (95% CI)
<b>Overall</b>	8.8 (7.9, 9.8)	1.9 (1.0, 2.7)
<b>Gender:</b>		
Males	6.5 (5.4, 7.7)	1.5 (0.7, 2.3)
Females	11.1 (9.7, 12.5)	2.2 (0.9, 3.5)
<b>Age (years):</b>		
50-64	9.0 (7.7, 10.3)	2.0 (0.9, 3.0)
65-74	8.5 (6.9, 10.0)	1.7 (0.6, 2.9)
≥75	9.1 (7.2, 11.0)	1.7 (0.6, 2.8)
<b>Males by Age (years):</b>		
50-64	7.2 (5.4, 9.0)	1.9 (0.7, 3.0)
65-74	5.6 (3.8, 7.4)	1.1 (-0.1, 2.3)
≥75	6.0 (3.5, 8.5)	1.1 (-0.3, 2.5)
<b>Females by Age (years):</b>		
50-64	10.8 (8.8, 12.8)	2.1 (0.5, 3.7)
65-74	11.4 (8.8, 14.0)	2.4 (0.8, 4.1)
≥75	11.4 (8.7, 14.1)	2.2 (0.2, 4.1)
<b>Socioeconomic status</b>		
Managerial & professional	6.2 (4.6, 7.9)	1.1 (-0.0, 2.2)
Intermediate	8.7 (6.6, 10.7)	1.4 (0.2, 2.7)
Routine & manual	9.7 (8.3, 11.0)	2.1 (0.8, 3.4)
Other*	9.6 (6.2, 13.0)	2.7 (-0.3, 5.8)
<b>Males by socioeconomic status</b>		
Managerial & professional	3.9 (2.2, 5.6)	0.6 (-0.4, 1.6)
Intermediate	7.0 (4.3, 9.7)	1.3 (-0.2, 2.7)
Routine/ manual	7.6 (5.8, 9.3)	1.9 (0.6, 3.2)
Other*	6.3 (1.9, 10.7)	1.9 (-1.1, 5.0)
<b>Females by socioeconomic</b>		
Managerial & professional	9.5 (6.5, 12.6)	1.8 (-0.1, 3.7)
Intermediate	10.2 (7.2, 13.2)	1.6 (-0.2, 3.4)
Routine & manual	11.7 (9.8, 13.7)	2.3 (0.5, 4.0)
Other*	11.3 (7.0, 15.5)	3.1 (-0.6, 6.9)
<b>Age 50-64 years by</b>		
Managerial & professional	6.1 (3.9, 8.3)	0.9 (-0.3, 2.2)
Intermediate	8.2 (5.4, 11.0)	1.6 (-0.0, 3.2)
Routine & manual	9.9 (8.0, 11.7)	2.2 (0.7, 3.6)
Other*	11.6 (5.8, 17.5)	3.9 (-1.1, 8.9)
<b>Age 65-74 years by</b>		
Managerial & professional	6.6 (3.5, 9.7)	1.5 (-0.4, 3.5)
Intermediate	7.7 (4.0, 11.3)	0.9 (-0.7, 2.6)
Routine & manual	8.9 (6.7, 11.1)	1.9 (0.3, 3.5)

Other*	11.1 (5.5, 16.6)	2.6 (-2.1, 7.4)
<b>Age ≥75 years by</b>		
Managerial & professional	6.1 (2.3, 9.9)	1.0 (-0.9, 2.8)
Intermediate	11.9 (6.8, 17.0)	2.0 (-0.7, 4.6)
Routine & manual	10.5 (7.7, 13.4)	2.2 (0.4, 4.0)
Other*	4.8 (1.4, 8.1)	1.0 (-0.8, 2.8)

328 \* The 'other' category includes housewives and individuals whose occupational class could not be  
329 determined or was inadequately described. CI: Confidence interval; SR: Symptomatic radiographic; OA:  
330 Osteoarthritis.

331

## 332 Discussion

333 Through both a systematic review and cross-sectional epidemiological study, this paper aimed to identify  
334 the population prevalence of radiographic ankle OA. The systematic review found that radiographic ankle  
335 OA has been previously under-researched in a community-dwelling setting. There was heterogeneity in the  
336 methods of assessing and defining the presence of radiographic ankle OA and general population  
337 prevalence estimates of radiographic ankle OA were not found within the existing literature. In our  
338 population of community-dwelling older adults aged 50 years and over, the period prevalence of 11.7% was  
339 found for ankle pain and 3.4% for symptomatic radiographic ankle OA. Stratified estimates found that the  
340 prevalence of both ankle pain and symptomatic radiographic ankle OA was higher in females, but lower in  
341 older age groups. Ankle pain and symptomatic radiographic ankle OA were also more prevalent in routine  
342 and manual occupations compared with managerial professions.

343  
344 The systematic review demonstrates that there is little published literature available for ankle OA in the  
345 community-dwelling populations. In comparison, previous systematic reviews of studies examining  
346 radiographic OA in the general population have all found greater numbers of published studies pertaining  
347 to the hand (176) [8], hip (23) [6], and foot (27) [9]. In addition, there were 190 epidemiological studies that  
348 used the Kellgren and Lawrence grading system alone to assess knee OA [7]. This systematic review also  
349 showed that no consistent method of assessment for radiographic ankle OA has been used and  
350 consequently the definitions of ankle OA varied greatly. Reviews of radiographic OA at other joint sites  
351 have found the Kellgren and Lawrence scale to be the most commonly used method of assessment [6,8,9].  
352 However, in the current systematic review only two studies used this scale [27,30], with the commonest  
353 form of assessment being the use of selected individual radiographic features. In addition to the limitations  
354 that have been noted for the Kellgren and Lawrence system [43] and variations in the interpretation of the  
355 scale [7], this could also be due to the recognition that the presentation of OA varies at different joint sites.  
356 For example, malalignment and erosion of the central cortical bone can be present in the hand joints [44],  
357 thickening of the medial femoral calcaneum and flattening of the femoral head at the hip, and medial tibial



358 attrition at the tiobiofemoral joint [45]. To address these issues, joint-specific scoring scales and atlases  
359 have been developed and are available for the hands, hips and knee joints, and more recently, the foot.  
360 However, at the time of the review none were available for the ankle, except the Bargon Arthrosis score  
361 which is a global scoring system developed to assess post-surgical complications [33,40,44-46]. The other  
362 atlases identified in the systematic review had all been adapted for use in the ankle or adapted for use in  
363 OA [20,31,32].

364

365 The prevalence of radiographic ankle OA was infrequently reported by studies and none were applicable to  
366 a general population. Published prevalence estimates ranged from 0.0% to 97.1%, the range and very high  
367 estimates are reflected by the selected populations and comparator groups examined as well as differences  
368 in the ages groups examined and methods used to assess radiographic ankle OA. As most of the selected  
369 populations were associated with sporting groups, it is likely that the high prevalence estimates in these  
370 studies would be much higher due to increased injury rates leading to post-traumatic forms OA compared  
371 to general populations. Therefore, owing to the heterogeneity of populations, methods of assessment and  
372 definitions of radiographic ankle OA, an overall prevalence estimate could not be derived from the studies  
373 in this systematic review. Additionally, it was not possible to examine stratified prevalence estimates for  
374 factors such as age and gender, unlike previous reviews of radiographic foot [9], hip [6,47] and knee OA  
375 [48].

376

377 The systematic review highlights the novelty of the prevalence estimate of 3.4% for symptomatic  
378 radiographic ankle OA in a community-dwelling population provided by our study. This estimate is similar  
379 to the reported prevalences of self-reported ankle pain (assumed to be symptomatic ankle OA) in retired  
380 football players and self-reported ankle OA in a general Australian population of 2.6% and 4%, respectively.  
381 However, these are both point prevalence estimates which either lack a true general population sample or  
382 the use of statistical methods to extrapolate prevalence estimates back to the general population, as  
383 employed in our study [13,49].

384

385 When compared with symptomatic radiographic OA at the hand (15.0%), hip (6.2%), knee (12.0%) and foot  
386 (16.7%) [35,50,51], our prevalence estimate for symptomatic radiographic ankle OA (3.4%) is significantly  
387 lower. One reason for this may be differences in the anatomical and biomechanical properties of cartilage  
388 at the ankle joint, which may be more resilient compared to other joints [52]. Radiographic grade $\geq$ 2, which  
389 was a required part of our definition of symptomatic radiographic ankle OA, is comparable to the definition  
390 used for foot OA [35] but is a higher threshold than tends to be used for radiographic knee, hip and hand  
391 OA and could explain our estimate at the ankle in comparison to these sites [50,51]. An estimate of 8.8%  
392 was obtained using a lower threshold of severity (grade $\geq$ 1) for symptomatic radiographic ankle OA, which is  
393 still lower than estimates of hand or knee OA, but higher than hip OA. This suggests that our prevalence  
394 estimate of 3.4% using the cut-off of grade $\geq$ 2 could be considered to be an estimate of moderate to severe  
395 symptomatic radiographic ankle OA. Previous estimates for ankle pain in general adult populations range  
396 from 9% [4] to 15% [5], although the populations in these studies were more restricted in age (25 years and  
397 over, and 65 years and over, respectively) and these studies employed different time periods over which  
398 the occurrence of ankle pain was captured (12 month and one month respectively).

399  
400 The prevalence of both ankle pain and symptomatic, radiographic ankle OA was slightly higher in females  
401 than males. Increased prevalence of ankle pain in females as also noted in the previous ankle pain studies,  
402 but may reflect previous findings that females are more likely and willing than men to report pain [4,5,53-  
403 56]. This gender pattern, while not previously examined in the general population at the ankle, is observed  
404 in knee and hand OA but is less marked at the hip [50,57,58]. Gender differences could be due to referred  
405 pain or biomechanical consequences of other conditions such as hallux valgus and ankle sprains, both of  
406 which are also known to have a higher prevalence in females [59,60]. In addition, there is also the increased  
407 risk of OA identified in older women that is thought to be due to the reduction in post-menopausal  
408 oestrogen production [58,61]. The higher prevalence estimates of ankle pain and slightly higher estimates  
409 of symptomatic radiographic ankle OA in adults aged 50-64 years contradicts other studies which report a  
410 positive association between age and the prevalence of symptomatic radiographic OA [47,62,63,64].  
411 However, decreases in prevalence of joint pain and OA in older ages has been reported, though less

412 commonly [4,47,65]. Older age is unlikely to affect structural changes observed radiographically, but may  
413 affect the reporting of pain due to stoicism, altered perception of pain or poor recall [66]. However, it is  
414 also possible that there is more pronounced healthy cohort effect in older participants who took part in the  
415 study. No previous studies have investigated the prevalence trends for ankle pain and socioeconomic  
416 status, however the increased prevalence in routine and manual occupational classes found in this study is  
417 consistent with patterns seen for other musculoskeletal pain and OA [55,67]. This is likely to be due to the  
418 high physical demands and heavy workloads experienced by employees in manual and routine occupations.

419

420 While we examined the effect of person-level risk factors (age, gender and socioeconomic status) have on  
421 ankle OA prevalence there are other notable joint-level risk factors that should be acknowledged for ankle  
422 OA. Previous injury or trauma to the ankle or surrounding structures has been recognised as an important  
423 localised risk factor for the subsequent development of ankle OA [68]. However, this study was undertaken  
424 in patients from a tertiary orthopaedic department and may have been affected by selection bias. In  
425 addition to this, OA and malalignment at the knee have been associated with degenerative changes at the  
426 contralateral ankle [69]. This is thought to be due to the changes in alignment and weight distribution that  
427 occur secondary to the OA process as well as accompanying pain symptoms [69].

428

429 The overall prevalence of ankle pain (11.7%) is significantly higher than the prevalence of symptomatic,  
430 radiographic ankle OA (3.4%). Comparing prevalence estimates for definitions of joint pain and  
431 symptomatic radiographic OA at the knee also shows similar trends [70]. Similar results for the ankle joint  
432 are also demonstrated in a study investigating the prevalence of ankle pain and self-reported OA in a  
433 population of retired footballers [13]. It is possible that ankle pain may be attributable to other pathologies  
434 occurring at the joint site or in surrounding structures, for example ligamentous or tendon injury, ankle  
435 sprain, or referred pain from other areas. However, it is also possible that pathophysiological changes are  
436 present but that the OA bony changes visible on radiographs are not yet present or detectable as this  
437 imaging method is known to be less sensitive than other imaging methods [71]. Other more sensitive

438 imaging modalities such as Magnetic Resonance Imaging (MRI) that allow the visualisation of soft tissue as  
439 well as more detailed views of the joint may identify higher prevalence estimates of ankle OA.

440

441 The strengths of this systematic review include a robust search strategy and application of inclusion and  
442 exclusion criteria. In addition, translation was used for non-English language papers rather than exclusion  
443 and authors of the publications were contacted where necessary to seek clarification. However, this  
444 systematic review used a single reviewer for title, abstract and full-text screening as well as quality  
445 appraisal and data extraction, increasing the risk of errors and bias. Additionally, publication bias was not  
446 considered as estimates of the prevalence of any condition are much less likely to be affected by publication  
447 bias as statistical significance is not a major consideration and we were not able to undertake any meta-  
448 analysis due to heterogeneity of the studies.

449

450 The cross-sectional secondary analysis included census sampling to recruit adults aged 50 years and over.  
451 This, along with the large sample size and similar age and gender distributions to the National Census 2011,  
452 gives greater confidence in the generalizability of the results of this study [35,71]. The standardised  
453 methods that were used to obtain weight-bearing AP and lateral views of the ankle and the scoring system  
454 including atlas were fully specified. A combined symptomatic and radiographic case definition was used and  
455 explicitly stated. Statistical methods used to account for missing data and non-response bias provided a full  
456 dataset for secondary analysis and allowed overall prevalence estimates to be calculated for the total  
457 eligible target population.

458

459 There are also a number of limitations which should be acknowledged. Most importantly, radiographic  
460 ankle data were only collected for those who reported pain in and around the foot in the last year. It is  
461 possible that not all responders may have perceived the ankle as being part of the foot. However,  
462 sensitivity analysis found that less than 2% of individuals who reported ankle pain on a whole body pain  
463 manikin in the last one month did not report pain in or around the foot in the last year (data not shown).  
464 Secondly, previous injury of the ankle was not examined in this study, and so the prevalence of ankle OA

465 attributable to this a potentially major risk factor for ankle OA could not be determined [68]. Thirdly, the  
466 restricted number of variables used within the weighted logistic regression model may mean that other  
467 factors that could have influenced response to the initial baseline health survey questionnaire have not  
468 been accounted for. Fourthly, while the intra-rater agreement for the presence of ankle OA was excellent,  
469 inter-rater agreement was found to be fair. The markedly lower inter-rater agreement is comparable or  
470 only slightly lower than agreement that has been previously reported in a recently developed ankle atlas  
471 [72], the original foot atlas [40] and the assessment of foot OA in the same population. The inter-rater  
472 agreement does vary at large joint sites such as the hip and knee [73,74], but also in other small joint sites  
473 such as the hands [75]. However, the ankle may be particularly challenging to score due to difficulties  
474 eliminating talar tilt and rotation and it has been noted that the levels of severity can vary across different  
475 regions of the joint [72]. As the second assessor scored radiographs only for reliability purposes and only  
476 scores from a single reader, who had excellent intra-rater agreement, were used for the main analysis,  
477 differences in interpretation of the atlas would not have led to differential classification of ankle OA within  
478 the study. However, given that the single main assessor was more conservative in their approach to  
479 scoring, the population prevalence estimates may have been underestimated. Additionally, although the  
480 CASF study population has been shown to be representative of the UK general population, there is under-  
481 representation of ethnic minority groups when compared to proportions in the overall UK population [71].

482

483 In summary, from the findings of the systematic review it can be concluded that there is a lack of existing  
484 research on ankle OA within the community-dwelling setting and great heterogeneity was seen between  
485 these existing studies in the radiographic assessment and definitions for ankle OA that were used. Ankle  
486 pain affected one in nine individuals in a community-based sample of older adults whereas symptomatic  
487 radiographic ankle OA occurred much less frequently affecting approximately one in 29 individuals.  
488 Radiographic joint changes therefore only explain a small proportion of those with pain, further  
489 investigations of the prevalence of ankle OA using more sensitive imaging modalities are warranted.

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498

## 499 **Conflict of Interest Statement**

500 The authors declare no conflicts of interest.

501

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508

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- 680

681 **Supporting Information**

682 **S1 File. PRISMA 2009 Checklist**

683 **S2 File. Radiographic Classification Atlas of Ankle Osteoarthritis**

684



## Supplementary File 1. PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title page, p.1
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	p.2
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	p.3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	p.4
<b>METHODS</b>			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	MPhil Thesis, Keele University ( <a href="http://www.keele.ac.uk//research/currentpgrstudents/theses/etheses/etheses-deposit/">www.keele.ac.uk//research/currentpgrstudents/etheses/etheses-deposit/</a> )
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	p.4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	p.4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	p.4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	p.4-5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	p.4-5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	p. 4-5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	p. 4-5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	p. 4-5

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$ ) for each meta-analysis.	n/a
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Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	p. 4-5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	p. 4-5
<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	p. 5
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	p. 5-6 & Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	p. 5-6, 10 & Table 1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	p. 5-6, 10 & Table 1
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n/a
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	p. 5-6, 10 & Table 1
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	p. 5-6 & Table 1
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	p. 17-21
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	p.20-21
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	p. 17-21
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	p.22

687

688 Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097.  
689 10.1371/journal.pmed1000097. For more information, visit: [www.prisma-statement.org](http://www.prisma-statement.org).

690



691 **Supplementary File 2. Radiographic Classification Atlas of Ankle**  
692 **Osteoarthritis**

693

694 Scoring system

- 695 • Ankle (anterior-posterior): osteophytes
- 696 • Ankle (anterior-posterior): joint space narrowing
- 697 • Ankle (lateral): osteophytes
- 698 • Ankle (lateral): joint space narrowing

699

700 Osteophytes

- 701 • 0 - absent
- 702 • 1 - small
- 703 • 2 - moderate
- 704 • 3 - severe

705

706 Joint space narrowing

- 707 • 0 - none
- 708 • 1 - definite
- 709 • 2 - severe
- 710 • 3 - joint fusion at least one point

711

712 Case definition

- 713 • Radiographic OA can be considered to be present if a score of 2 or above is documented for either
- 714 osteophytes or joint space narrowing, from either the anterior-posterior or lateral view

715

716

# Anterior-posterior view - osteophytes

717



0



1



2



3

718

# Anterior-posterior view – joint space narrowing

719



0



1

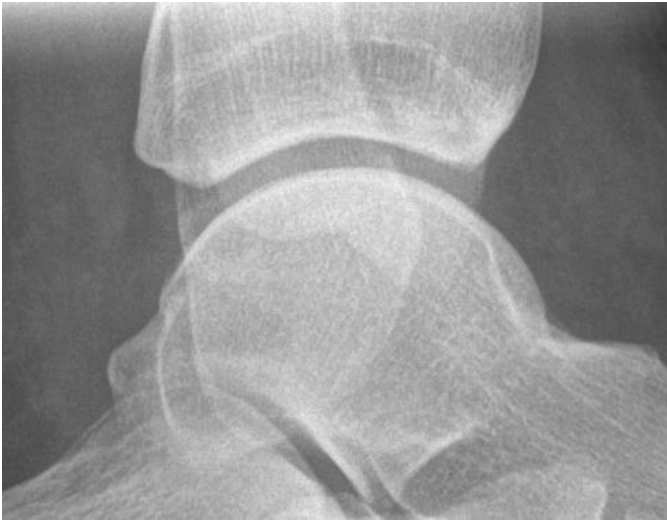


2

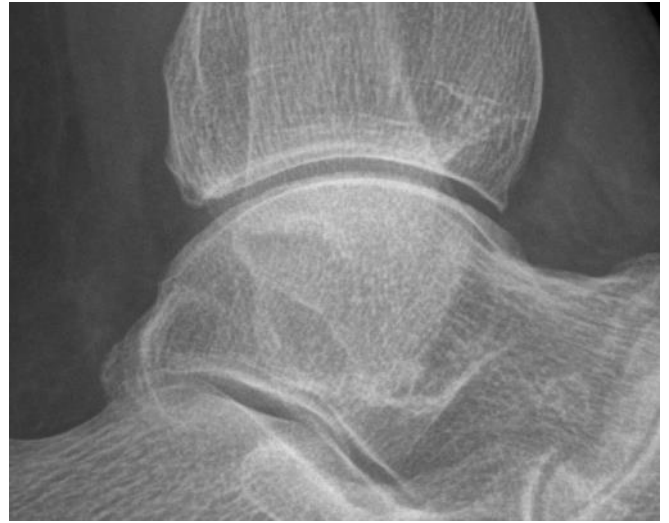


3

# Lateral view - osteophytes



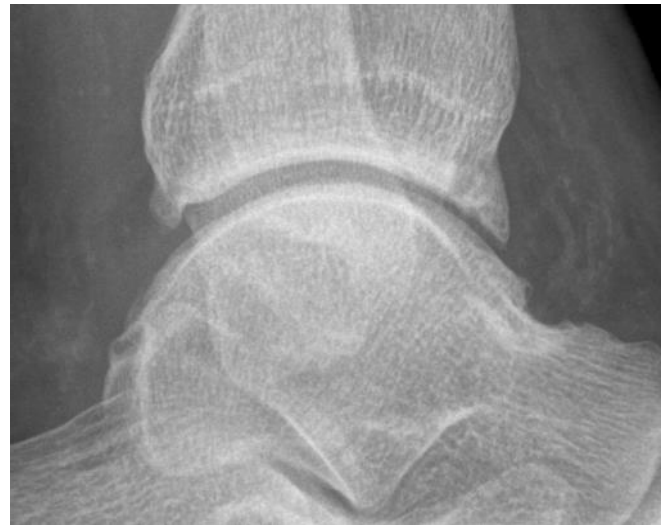
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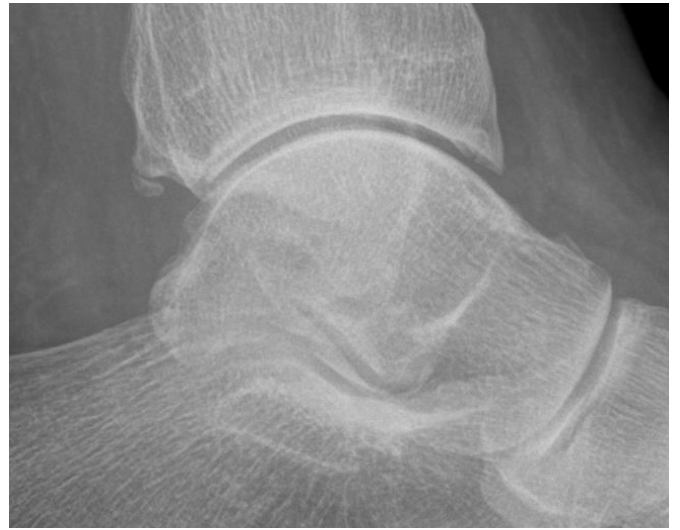


3

# Lateral view – joint space narrowing



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1



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