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1 **Midfoot osteoarthritis: potential phenotypes and their associations with**
2 **demographic, symptomatic and clinical characteristics**

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23

24 **ABSTRACT**

25 **Objective**

26 To investigate the demographic, symptomatic, clinical and structural foot
27 characteristics associated with potential phenotypes of midfoot osteoarthritis (OA).

28 **Design**

29 Cross-sectional study of 533 community-dwelling adults aged ≥ 50 years with foot
30 pain in the past year. Health questionnaires and clinical assessments of symptoms,
31 foot structure and function were undertaken. Potential midfoot OA phenotypes were
32 defined by the pattern of radiographic joint involvement affecting either the medial
33 midfoot (talonavicular, navicular-1st cuneiform, or cuneiform-1st metatarsal joint),
34 central midfoot (2nd cuneiform-metatarsal joint), or both medial and central midfoot
35 joints. Multivariable regression models with generalised estimating equations were
36 used to investigate the associations between patterns of midfoot joint involvement
37 and symptomatic, clinical and structural characteristics compared to those with no or
38 minimal midfoot OA.

39 **Results**

40 Of 879 eligible feet, 168 had medial midfoot OA, 103 central midfoot OA, 76 both
41 medial and central midfoot OA and 532 no/minimal OA. Having both medial and
42 central midfoot OA was associated with higher pain scores, dorsally-located midfoot
43 pain (OR 2.54, 95%CI 1.45, 4.45), hallux valgus (OR 1.76, 95%CI 1.02, 3.05), flatter
44 foot posture (β 0.44, 95%CI 0.12, 0.77), lower medial arch height (β 0.02, 95%CI
45 0.01, 0.03) and less subtalar inversion and 1st MTPJ dorsiflexion. Isolated medial
46 midfoot OA and central midfoot OA had few distinguishing clinical characteristics.

47 **Conclusions**

48 Distinct phenotypes of midfoot OA appear challenging to identify, with substantial
49 overlap in symptoms and clinical characteristics. Phenotypic differences in
50 symptoms, foot posture and function were apparent in this study only when both the
51 medial and central midfoot were involved.

52 **Keywords:** foot, osteoarthritis, phenotype, midfoot, pain, function

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77 INTRODUCTION

78 Foot osteoarthritis (OA) is increasingly recognised as an important contributor to the
79 burden of OA, affecting 1 in 6 adults aged over 50 years, with a significant negative
80 impact on physical mobility and quality of life¹⁻³. The most commonly affected foot
81 joint is the first metatarsophalangeal (1st MTP; 7.8%), followed by the midfoot,
82 including the second cuneiform-metatarsal (2nd CMJ; 6.8%), talonavicular (TNJ;
83 5.8%), navicular-first cuneiform (NCJ; 5.2%) and first cuneiform-metatarsal joints (1st
84 CMJ; 3.9%)¹.

85 Midfoot OA has been recognised as a distinct subtype of foot OA, with recent
86 findings indicating the presence of two main phenotypes of radiographic foot OA
87 based on the pattern of joint involvement⁴. The first is isolated 1st MTPJ OA with
88 minimal midfoot involvement, and the second is polyarticular OA affecting both the 1st
89 MTPJ and midfoot joints (TNJ, NCJ and CMJs). Polyarticular foot OA is the most
90 disabling form of foot OA⁴ and is associated with foot pain, obesity, previous injury,
91 lower medial arch height and pain in other weight-bearing joints^{2, 4, 5}. The significant
92 impact that midfoot OA has on physical function is, in part, attributed to the important
93 role the midfoot has in distributing load in the foot during weight-bearing activities
94 such as walking⁶, standing⁷ and stair climbing⁸. Progression towards significant flat-
95 foot deformity with advanced midfoot OA also results in complaints of unusual foot
96 posture and difficulty with footwear fitting⁹.

97 Because the midfoot has a complex structure with many articulations, it is possible
98 that distinct patterns of involvement exist. Indeed, results from a data-driven
99 approach used to identify subgroups of foot OA from a large, population-based
100 cohort identified two main clusters of foot OA (polyarticular and 1st MTPJ), and raised
101 the possibility of two subsets of midfoot OA existing; one affecting the medial midfoot

102 joints only (TNJ, NCJ or 1st CMJ) and the other the central midfoot only or 'second
103 ray' (2nd CMJ)⁴.

104 The potential presence of two subgroups of midfoot OA may be explained, in part, by
105 differences in the function of the medial versus central joints of the midfoot. The most
106 medial part of the midfoot, involving the joints along the medial arch such as the TNJ,
107 1st NCJ, and 1st CMJ (first ray), is highly mobile during walking and becomes loaded
108 dorsally when the arch flattens⁶. This is in contrast to the 2nd CMJ which contributes
109 less to medial arch stability, is tightly bound, and displays minimal motion^{7, 10}.

110 Anatomically, the 1st CMJ and 2nd CMJ also typically have separate synovial
111 compartments^{11, 12} further reinforcing their distinction as separate functional entities
112 in the medial and central regions of the midfoot. It is therefore plausible that the
113 mechanisms underlying the development of these two subgroups of midfoot OA
114 differ, which may be reflected in the clinical and structural foot characteristics
115 observed in clinical practice. Existing studies have not been able to adequately
116 investigate patterns of OA within the midfoot and their associations with clinical
117 features due to a focus on either the tarsometatarsal or medial midfoot joints, small
118 sample sizes or a narrow range of measured clinical characteristics^{8, 13-17}. There
119 have been no prior studies investigating potential phenotypes specifically in the
120 midfoot, nor any association with clinical characteristics.

121 Characterising midfoot OA and potential phenotypes in greater detail will improve our
122 understanding of their clinical presentation and may offer early insights into the
123 mechanisms involved in disease pathogenesis. This line of research is also attractive
124 as a basis for developing targeted or stratified interventions for different types of foot
125 OA in the future, two areas identified as key OA research priorities by the European
126 League Against Rheumatism (EULAR)¹⁸. The aim of this study was to investigate the

127 demographic, symptomatic, clinical and structural foot characteristics associated with
128 potential phenotypes of midfoot OA based on different patterns of joint involvement;
129 medial midfoot OA only (TNJ, NCJ or 1st CMJ), central midfoot OA only (2nd CMJ)
130 and combined medial and central midfoot OA.

131 **METHODS**

132 *Study design and population*

133 This study was a cross-sectional analysis of baseline data from the Clinical
134 Assessment Study of the Foot (CASF), a large prospective observational cohort
135 study in North Staffordshire, UK¹⁹. Health Survey questionnaires were mailed to
136 patients aged 50 years and over registered with four general practices. Individuals
137 who responded and indicated they had foot pain in the last 12 months were invited to
138 attend a research clinic for a clinical assessment and plain radiography of both feet.
139 Participants were excluded from the current analyses if their medical records or
140 radiology report identified them as having inflammatory arthritis (rheumatoid arthritis,
141 psoriatic arthritis or non-specific inflammatory arthritis). All participants provided
142 written informed consent and ethical approval was granted for this study from
143 Coventry Research Ethics Committee (REC reference number: 10/H1210/5).

144 *Data Collection*

145 *Health Survey Questionnaire*

146 The Health Survey questionnaire included items on demographics and socio-
147 economic status (age, sex, education, occupation), general health, foot pain and
148 symptoms (pain in the last 12 months, pain severity in the last month using a 0-10
149 numerical rating scale [NRS], duration of pain, and the Manchester Foot Pain and
150 Disability Index (MFPDI)²⁰). Foot pain location was recorded by participants marking

151 or shading the corresponding area on a foot manikin^{21, 22} (© The University of
152 Manchester 2000, all rights reserved). Dorsal and plantar midfoot pain were then
153 determined according to the region(s) selected. Raw MFPDI pain and function scores
154 were converted to Rasch-transformed logit values for statistical analysis²³. The
155 presence of hallux valgus was determined from validated self-report line drawings
156 obtained during the questionnaire²⁴, with the three most severe depictions graded as
157 present and the two least severe as absent²⁵.

158 *Clinical assessment*

159 Physical and clinical assessments (foot posture, range-of-motion and deformity) were
160 undertaken on all participants who attended the research clinic according to
161 standardised protocols by one of seven trained therapists (podiatrist or
162 physiotherapist)¹⁹. Pre-study training and quality control measures were undertaken
163 throughout the study¹⁹. Anthropometric measurements (height and weight) were
164 taken, and body mass index (BMI) subsequently derived. Foot posture was assessed
165 with participants in a relaxed standing position using the Foot Posture Index (FPI)²⁶,
166 Arch Index (AI)²⁷ and Navicular Height (NH), with NH being normalised to the total
167 foot length²⁸. The FPI is a six-item observational rating tool for the assessment of
168 overall foot posture, with each item corresponding to an individual feature and graded
169 from -2 (supinated) to +2 (pronated) for maximum scores ranging from -12 (highly
170 supinated) to +12 (highly pronated)²⁶. Raw scores were converted to Rasch-
171 transformed logit values for statistical analysis²⁹. The AI was derived from carbon
172 paper footprints and is defined as the ratio of the area of the middle third of the foot
173 to the total footprint area (minus the toes)²⁷. Higher AI values indicate a more
174 flattened medial foot arch. Measurement of NH was taken by marking the navicular
175 tuberosity with a pen, measuring its height from the supporting surface with a ruler (in

176 millimetres), and dividing this value by the total length of the foot. Lower NH values
177 indicate a flatter medial foot arch²⁸. Values for the FPI and AI were also presented in
178 categories based on established cut-points^{30, 31}, with NH values categorised in tertiles
179 according to the variable distribution.

180 Range-of-motion at the ankle joint was assessed with an inclinometer using the
181 weight bearing lunge test with the knee flexed and extended^{32, 33}. Subtalar/ankle
182 inversion and eversion were assessed with the participant non-weight-bearing using
183 a goniometer³⁴. Non-weight bearing dorsiflexion range-of-motion of the 1st MTPJ was
184 also assessed using a flexible goniometer³⁵. Midfoot exostosis was documented as
185 the presence or absence of a bony prominence on the dorsum of the foot in non-
186 weight bearing. Reliability of foot posture and clinical tests has previously been
187 reported^{28, 32-35}.

188 *Radiographic assessment and scoring*

189 Participants had weight-bearing dorsoplantar and lateral radiographs of both feet
190 taken according to a standardised protocol³⁶. Radiographs were graded separately
191 for joint space narrowing (JSN) and osteophytes (OP) in four midfoot joints (TNJ,
192 NCJ, 1st CMJ and 2nd CMJ) and the 1st MTPJ by a single reader (M.M.).

193 Radiographic OA of a foot joint was defined as grade ≥ 2 for osteophytes (OP) or joint
194 space narrowing (JSN) on either dorsoplantar or lateral views, as previously
195 described³⁶. Intra- and inter-observer reliability (MM and HBM) for scoring within this
196 dataset have previously been reported as excellent (mean unweighted $\kappa = 0.94$,
197 mean % agreement 99%) and moderate (mean unweighted $\kappa = 0.46$, mean %
198 agreement 79%), respectively¹.

199 Four mutually exclusive groups were defined according to the presence of
200 radiographic OA in the midfoot joints of each foot (Figure 1):

201 (1) Medial midfoot OA only: grade ≥ 2 for JSN or OP in *either* the TNJ or NCJ or
202 1st CMJ, with no OA (grade ≤ 1) in the 2nd CMJ.

203 (2) Central midfoot OA only: grade ≥ 2 for JSN or OP in the 2nd CMJ only, with no
204 OA (grade ≤ 1) in the TNJ, NCJ and 1st CMJ.

205 (3) Combined medial and central midfoot OA: grade ≥ 2 for JSN or OP in both the
206 medial midfoot (at least one of the TNJ, NCJ or 1st CMJ) *and* central midfoot
207 (2nd CMJ). This group was included to ensure feet with OA involvement across
208 both regions were included, as we anticipated a significant number of feet with
209 more extensive involvement.

210 (4) No or minimal OA: No OA of the midfoot (grade ≤ 1) for JSN or OP for the TNJ,
211 NCJ, 1st CMJ and 2nd CMJ.

212 ***Figure 1 here***

213 *Statistical analysis*

214 Differences between midfoot OA phenotypes were assessed using multivariable
215 linear regression for continuous outcomes and binary logistic regression for
216 dichotomous outcomes. All necessary assumptions for the analyses were tested for
217 and met. Analyses were foot-based, with generalised estimating equations used to
218 account for between foot correlations within each person and adjusted for age, sex
219 and BMI. Further adjustment was also made for the presence of 1st MTPJ OA. An
220 exchangeable working correlation structure was specified for the analysis given the
221 lack of time-dependent or logical ordering of the data. The no or minimal OA group
222 were designated as the reference category. Results for continuous outcomes are

223 presented as adjusted unstandardised regression coefficients (β) and considered
224 statistically significant if the 95% confidence intervals (CI) did not include 0. For
225 dichotomous outcomes, results are presented as adjusted odds ratios (ORs) with
226 95% CI and were considered statistically significant if the 95% CI did not include
227 1.00. All analyses were conducted using SPSS (v21, IBM Corporation, NY, USA).

228 **RESULTS**

229 *Descriptive characteristics*

230 Five hundred and sixty people attended the research assessment clinics, of whom 24
231 had inflammatory arthritis and three did not have foot radiographs, leaving 533
232 eligible clinic attenders for analysis (mean age 64.9 years SD [8.4], 55% female).

233 Of the 1066 feet, 532 had no or minimal OA of the midfoot (49.9%), 168 had medial
234 midfoot OA only (15.7%), 103 had central midfoot OA only (9.6%), and 76 had
235 combined medial and central midfoot OA (7.1%). Isolated OA of the 1st MTPJ
236 occurred in 175 feet and with radiographic data were missing for 12 1st MTP joints
237 (not included in analyses). Compared to the midfoot OA groups, those with isolated
238 1st MTPJ OA tended to be similar for age, BMI and proportion attending higher
239 education; whilst having a higher proportion in manual occupations and less self-
240 reported foot pain and better foot function (data not shown). The prevalence of
241 concurrent 1st MTPJ OA in feet with midfoot OA was 15% (n=134). In feet with medial
242 midfoot OA, the TNJ was most commonly affected (70%), followed by the NCJ (21%)
243 and 1st CMJ (19%). In feet with medial and central OA, the most common joints with
244 OA were the 2nd CMJ (100%) and NCJ (63%), followed by the TNJ (46%) and 1st
245 CMJ (22%). Twenty of the 879 feet in the analysis (2.2%) had no radiographic
246 changes (0 for OP or JSN).

247 Summary statistics for person and foot-level characteristics according to the different
248 patterns of midfoot OA involvement are presented in Table 1. Individuals with
249 combined medial and central midfoot OA tended to be older, had a higher BMI, a
250 longer duration of symptoms, a higher proportion with manual occupations and a
251 higher proportion of females compared to the no or minimal midfoot OA group. Those
252 with central midfoot OA only tended to be older, and those with medial midfoot OA
253 only had a higher BMI compared to the no or minimal midfoot OA group.

254 ***Table 1 here***

255 *Clinical characteristics*

256 Multivariable associations between clinical characteristics and midfoot OA groups
257 adjusted for age, sex, BMI and presence of 1st MTPJ OA are presented in Table 2.
258 For clarity, only fully adjusted models are presented (partially adjusted regression
259 models for age, sex and BMI are also provided in Supplementary File 1 for
260 completeness).

261 Following adjustment for age, sex, BMI and presence of 1st MTPJ OA, the combined
262 medial and central midfoot OA group was more likely to report dorsally-located
263 midfoot pain (OR 2.54; 95% CI 1.46, 4.44), and hallux valgus (OR 1.76; 95% CI 1.02,
264 3.05) and had higher MFPDI pain scores indicating worse pain ($\beta = 0.004$, 95% CI
265 0.0000002, 0.008) compared to the no or minimal OA group. They also displayed a
266 flatter foot posture, with higher FPI ($\beta = 0.44$; 95% CI 0.12, 0.77) and AI scores ($\beta =$
267 0.02; 95% CI 0.01, 0.03) and lower navicular height ($\beta = -0.01$; 95% CI -0.01, -0.002),
268 and had less subtalar inversion ($\beta = -2.45$; 95% CI -4.41, -0.48) and 1st MTPJ
269 dorsiflexion ($\beta = -4.30$; 95% CI -8.38, -0.21). Differences in pain severity and foot
270 posture were relatively small in magnitude compared to the no or minimal OA group.

271 Central midfoot OA was associated with higher MFPDI pain scores ($\beta = 0.004$; 95%
272 CI 0.0002, 0.008), a higher AI (flatter medial arch) ($\beta = 0.010$; 95% CI 0.000002,
273 0.02) and less ankle joint dorsiflexion ($\beta = -1.464$; 95% CI 2.924, -0.005) compared to
274 the no or minimal OA group, with the magnitude of these associations representing
275 small effects. The strength of the association between those with central midfoot OA
276 and the likelihood of reporting dorsal midfoot pain compared to the no or minimal OA
277 group was similar, but less precise, versus the same association for the combined
278 medial and central OA group (OR 1.59; 95% CI 0.95, 2.66, $P = 0.078$).

279 Medial midfoot OA was associated with increased likelihood of reporting dorsally
280 located midfoot pain (OR 1.54; 95% CI 1.02, 2.33) and less subtalar inversion ($\beta = -$
281 1.715; 95% CI -2.955, -0.474) compared to the no or minimal OA group. The
282 direction of association for ankle joint dorsiflexion and subtalar inversion was
283 opposite for the medial midfoot OA group compared to the central and combined
284 medial and central groups, with greater ankle joint dorsiflexion and less subtalar
285 inversion.

286 ***Table 2 here***

287

288 **DISCUSSION**

289 This study aimed to investigate the demographic, symptomatic, clinical and structural
290 foot characteristics associated with different phenotypes of midfoot OA. Previous
291 findings have alluded to different phenotypes based on the pattern of joint
292 involvement affecting either the medial or central regions of the midfoot. We therefore
293 hypothesized that the differences in joint involvement may be reflected in the clinical
294 and structural foot characteristics observed in clinical assessments. Overall, OA

295 affecting both the medial and central midfoot joints was associated with differences in
296 symptoms, foot posture and range-of-motion compared to the no/minimal foot OA
297 group. Overlap in the clinical characteristics of isolated medial or central midfoot OA
298 were observed, making it challenging to differentiate these presentations on the basis
299 of their symptoms and clinical information alone.

300 Midfoot OA is associated with significant pain-related disability^{2, 4}, alterations to
301 midfoot alignment¹³ and reduced range-of-motion during movement⁸. In this study,
302 high levels of foot pain-related disability were observed in the presence of OA across
303 the combined medial and central midfoot regions, expanding on our previous
304 findings⁴. Pain was more likely to be situated in the dorsal midfoot region,
305 representing a new finding regarding the localisation of pain in people with midfoot
306 OA. This is most likely explained by the close proximity of the midfoot joints to the
307 dorsal aspect of the foot, and aggregation of bony and soft tissue changes near the
308 joint surface³⁷.

309 Differences in clinical measures of foot structure such as a flatter medial longitudinal
310 arch were also observed in this study, consistent with studies using radiological
311 measures^{13, 38}. Combined with higher maximum forces and pressures under the
312 midfoot during walking in people with midfoot OA^{13, 14}, these changes may have
313 implications for performing activities that place significant load through the midfoot
314 such as stair climbing⁸ and have been shown to relate to levels of pain-related
315 disability¹⁴.

316 When OA was present in both the medial and central midfoot, individuals tended to
317 be older with a longer duration of symptoms compared to the other patterns of
318 midfoot OA. Changes to overall foot posture indicated by the FPI score and a flatter
319 medial arch were evident with involvement of both the medial and central midfoot

320 joints, whereas this was confined to a flatter medial arch in central midfoot OA. The
321 FPI captures additional elements of foot position during standing such as abduction
322 of the forefoot and eversion of the hindfoot. This suggests the possibility that the
323 effect of midfoot OA on symptoms and foot structure may be cumulative and
324 progressive in nature, with differences observed once midfoot OA is present in both
325 medial and central regions, although prospective studies are needed. It is also
326 possible that this reflects a greater number of midfoot joints involved or greater
327 radiographic severity, although relationships between symptoms and clinical
328 characteristics with the extent of OA and radiographic severity are not always
329 consistent³⁹. Recent evidence suggests symptoms of midfoot OA across the medial
330 and central midfoot joints are persistent, with little change over 18 months⁴⁰. Further
331 study is required to determine whether joint involvement and foot structure in midfoot
332 OA changes longitudinally and whether this is related to symptoms.

333 This study also identified the presence of differences in foot function in people with
334 midfoot OA not previously reported, including less subtalar inversion and 1st MTPJ
335 dorsiflexion, and a higher likelihood of hallux valgus. These associated changes in
336 the feet more generally may imply a wider-reaching impact of midfoot OA on foot
337 function, with potential implications for the management of associated foot deformity.
338 Although evidence from prospective studies is lacking, associations between flat foot
339 posture with 1st MTPJ ROM, OA and hallux valgus have been reported⁴¹⁻⁴³. Given
340 that people with midfoot OA have flatter feet than those with no or minimal OA^{13, 16}, it
341 is possible that the mechanisms involved in the development of forefoot pathology
342 are common to flat feet and midfoot OA. However, the temporal sequence of such
343 proposed events cannot be determined from cross-sectional studies and prospective
344 investigation is required to explore the long-term sequelae of midfoot OA.

345 Contrary to our hypothesis, limited distinction in the clinical characteristics between
346 patterns of isolated medial and central midfoot OA were observed in this study. Only
347 small differences in range-of-motion at the ankle and subtalar joints were present,
348 with this varying very little (less than two degrees) according to the presence of
349 isolated medial or isolated central midfoot OA. Larger differences were seen for the
350 combined medial and central midfoot OA group, including measures of overall foot
351 posture, arch height, dorsal midfoot pain, presence of hallux valgus, subtalar
352 inversion and 1st MTPJ range-of-motion. Subsequently, identification of more
353 extensive midfoot OA based on these clinical features may be achieved with greater
354 confidence, with consistency of the findings across these outcomes. Although the
355 findings indicated a tendency for greater ankle dorsiflexion and less subtalar
356 inversion for medial midfoot OA, they do not offer any pertinent insights into potential
357 mechanisms of disease pathogenesis for different subsets of midfoot OA. Otherwise,
358 there was considerable overlap in clinical characteristics between feet with midfoot
359 OA in different regions. These findings mirror challenges identified in the
360 identification of potential phenotypes in other regions of small joint OA, such as the
361 hand^{44, 45}. Considerable overlap has been identified in symptoms, self-reported
362 function and strength according to the location and distribution of OA⁴⁴. From a
363 practical standpoint, our data suggests that it is difficult to differentiate between
364 isolated medial midfoot OA and isolated central midfoot OA on clinical grounds. The
365 findings of this study also provide insight into clinical features more likely to
366 distinguish combined medial and central midfoot OA, such as a more pronated
367 overall foot posture and reduced navicular height. Therefore at present, in the
368 absence of medical imaging, suspected midfoot OA affecting joints such as the NCJ,
369 1st CMJ and 2nd CMJ should probably be investigated approaching these joints as a

370 composite unit. It is also possible that phenotypes of midfoot OA based on the
371 pattern of joint involvement may not be detectable in the clinical setting, or that more
372 detailed information is required to identify them. Indeed, brief clinical assessments
373 perform poorly in diagnosing radiographic midfoot OA in individuals with midfoot
374 pain⁵, highlighting the additional complexities in distinguishing subsets of midfoot OA.
375 Recent studies of OA phenotyping at other joints with magnetic resonance imaging⁴⁶,
376 ⁴⁷, pain and psychological profiling⁴⁸⁻⁵⁰ and muscle strength assessment⁵¹ present
377 opportunities that could be applied to midfoot OA in future studies.

378 Strengths of this study include drawing on a large community-dwelling sample of
379 adults with foot OA and a wide range of documented clinical characteristics relating
380 to symptoms, foot structure and function. Generalised estimating equations were
381 used to maximise the available data from both feet, whilst accounting for between-
382 feet correlations within each person. The assessment items had well established
383 reliability (with the exception of lower inter-rater reliability for ankle/subtalar inversion
384 and eversion) and were reflective of the types of measurements commonly taken in
385 clinical practice. Whilst reliability testing was not performed formally during the study,
386 quality assurance and control were integral parts as detailed in the study protocol¹⁹.

387 There are also limitations to be considered when interpreting the findings of this
388 study. Midfoot OA subsets were based on the pattern of OA joint involvement in four
389 midfoot joints due to the availability of an established and reliable radiographic atlas
390 for these articulations. Involvement of other midfoot joints is possible and should be
391 explored further in future studies, although reliable scoring of other joints may be
392 problematic. Although there was a large number of total participants with foot OA, the
393 number in each of the subgroups was smaller, reducing statistical power. Participants
394 in this study also experienced foot pain in the past 12 months, therefore caution

395 should be taken extrapolating these findings to the wider population. Despite an array
396 of clinical assessment items being undertaken, items relating to pain at specific joints
397 in the midfoot upon palpation and movement may be more informative, albeit the
398 reliability and clinical utility of other tests is unclear. Lastly, the exploratory nature of
399 this analysis now warrants further investigation to substantiate the clinical
400 significance of differences in characteristics between subsets of midfoot OA.

401 In conclusion, this is the first detailed investigation exploring potential midfoot OA
402 phenotypes based on the pattern of joint involvement and their associated
403 demographic, symptomatic and clinical characteristics. Midfoot OA affecting both the
404 medial and central joints was associated with higher levels of foot-related pain, most
405 commonly located on the dorsal aspect of the midfoot. This was accompanied by a
406 flatter overall foot posture, lower medial longitudinal arch, less subtalar inversion and
407 1st MTPJ dorsiflexion. Limited distinguishing clinical characteristics existed between
408 patterns of OA present in the medial or central midfoot, highlighting challenges in the
409 identification of further subsets of midfoot OA in the clinical setting. Differences in
410 alignment of the medial arch may offer potential for distinguishing midfoot OA at
411 different sites and at different stages of disease development. Future studies are
412 warranted to track disease progression and joint involvement in midfoot OA over time
413 and the associated changes in symptoms and functional impairment.

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423 **AUTHOR CONTRIBUTIONS**

424 JBA, MJT, HBM and ER conceived and designed the study. MJT, MM and ER were
425 responsible for data acquisition. Analysis and interpretation of data was undertaken
426 by JBA, MM, MJT, AR, HBM and ER. All authors drafted or revised the article
427 critically for important intellectual content, and approved the final version of the
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446 The authors have no financial or other competing interests to declare.

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621 **Figure legends**

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623 **Figure 1.** Dorsoplantar radiographs depicting examples of patterns of joint
624 involvement for feet with no or minimal OA (A), medial midfoot OA affecting the NCJ
625 and TNJ (B), central midfoot OA in the 2nd CMJ (C), and combined medial and
626 central midfoot OA affecting the NCJ, 1st and 2nd CMJ (D).

Table 1. Person-level characteristics (age, sex, BMI, pain ratings, MFPDI) and foot-level characteristics for groups (n=879 feet)

	No or minimal foot OA (n=532)	Medial midfoot OA (n=168) TNJ or NCJ or 1 st CMJ (and no 2 nd CMJ)	Central midfoot OA (n=103) 2 nd CMJ only	Combined medial and central midfoot OA (n=76) TNJ or NCJ or 1 st CMJ & 2 nd CMJ
Age, years	63.7 (63.0, 64.4)	65.6 (64.2, 66.9)	66.9 (65.3, 68.6)	68.3 (66.6, 70.1)
Sex, % female	54.7 (50.5, 58.9)	50.6 (43.0, 58.2)	63.1 (53.8, 72.4)	75.0 (65.3, 84.7)
BMI (kg/m ²)	29.7 (29.3, 30.2)	31.2 (30.3, 32.1)	30.8 (29.8, 31.8)	32.7 (31.3, 34.0)
Manual occupation, %	51.3 (47.1, 55.6)	51.7 (44.2, 59.3)	46.6 (37.0, 56.2)	59.2 (48.2, 70.3)
Attended higher education, %	30.6 (26.0, 33.8)	21.6 (14.2, 26.3)	26.4 (17.7, 34.7)	18.6 (9.7, 27.1)
Joint specific OA				
Talonavicular joint (TNJ), <i>n</i> (%)	0 (0)	118 (70)	0 (0)	35 (46)
Navicular-first cuneiform (NCJ), <i>n</i> (%)	0 (0)	36 (21)	0 (0)	48 (63)
First cuneiform-metatarsal (1 st CMJ), <i>n</i> (%)	0 (0)	33 (19)	0 (0)	17 (22)
Second cuneiform-metatarsal (2 nd CMJ), <i>n</i> (%)	0 (0)	0 (0)	103 (100)	76 (100)
Foot pain and functional limitation				
Foot pain severity in last month (0-10 NRS)	5.1 (4.9, 5.3)	5.5 (5.1, 5.9)	5.3 (4.8, 5.7)	5.8 (5.2, 6.3)
Duration of pain, %				
< 12 months	16.8 (13.3, 20.0)	9.9 (5.0, 14.8)	12.5 (5.9, 19.1)	3.0 (0.0, 7.2)
1 to < 5 years	37.0 (32.5, 41.5)	39.4 (31.4, 47.5)	34.4 (24.9, 43.9)	25.8 (15.2, 36.3)
5 to < 10 years	16.3 (12.9, 19.8)	21.8 (15.0, 28.6)	28.1 (19.1, 37.1)	34.8 (23.4, 46.3)
≥ 10 years	29.9 (25.7, 34.2)	28.9 (21.4, 36.3)	25.0 (16.3, 33.7)	36.4 (24.8, 48.0)
MFPDI Pain Score	-0.292 (-0.424, -0.160)	-0.299 (-0.529, -0.069)	0.136 (-0.133, 0.406)	0.183 (-0.164, 0.529)
MFPDI Function Score	-0.807 (-0.986, -0.628)	-0.553 (-0.862, -0.244)	-0.370 (-0.736, -0.004)	0.188 (-0.302, 0.678)

Table 1 continued. Person-level characteristics (age, sex, BMI, pain ratings, MFPDI) and foot-level characteristics for groups (n=879 feet)

	No or minimal foot OA (n=532)	Medial midfoot OA (n=168) TNJ or NCJ or 1 st CMJ (and no 2 nd CMJ)	Central midfoot OA (n=103) 2 nd CMJ only	Combined medial and central midfoot OA (n=76) TNJ or NCJ or 1 st CMJ & 2 nd CMJ
Pain location and deformity				
Dorsal midfoot pain, %	23.3 (19.7, 26.9)	29.1 (22.3, 36.0)	30.0 (21.2, 39.0)	48.6 (37.4, 59.9)
Plantar midfoot pain, %	28.3 (24.6, 32.2)	26.1 (19.5, 32.8)	24.2 (16.0, 32.6)	13.1 (5.6, 20.8)
Midfoot bony exostosis, %	73 (68.8, 76.3)	60.7 (53.3, 68.1)	66.9 (57.9, 76.1)	59.2 (48.2, 70.3)
Hallux valgus, %	28.5 (24.7, 32.4)	33.9 (26.8, 41.1)	39.8 (30.4, 49.3)	48.6 (37.4, 59.9)
Concurrent 1 st MTPJ OA, %	3.7 (2.1, 5.4)	23.8 (17.4, 30.3)	46.6 (37.0, 56.1)	34.2 (23.5, 44.9)
Foot posture				
Foot Posture Index	2.4 (2.3, 2.6)	2.1 (1.8, 2.4)	2.9 (2.6, 3.3)	3.2 (2.8, 3.5)
Supinated (<0), n (%)	40 (7.5)	16 (9.5)	5 (4.9)	1 (1.3)
Normal (0-5)	326 (61.3)	111 (66.1)	57 (55.3)	43 (56.6)
Pronated (≥6)	166 (31.2)	41 (24.4)	41 (39.8)	32 (42.1)
Arch Index	0.236 (0.231, 0.240)	0.242 (0.234, 0.249)	0.268 (0.258, 0.277)	0.272 (0.262, 0.283)
Low arch (<0.21), n (%)	331 (62.2)	109 (64.9)	55 (53.4)	46 (60.5)
Normal (0.21-0.28)	75 (14.1)	30 (17.9)	36 (35.0)	26 (34.2)
High arch (>0.28)	126 (23.7)	29 (17.3)	12 (11.7)	4 (5.3)
Navicular height	0.175 (0.173, 0.178)	0.176 (0.171, 0.180)	0.162 (0.156, 0.168)	0.151 (0.143, 0.159)
High (>0.18-0.29), n (%)	185 (34.9)	51 (30.5)	32 (31.1)	21 (27.6)
Normal (>0.16-0.18)	153 (28.9)	48 (28.7)	45 (43.7)	43 (56.6)
Low (0.06-0.16)	192 (36.2)	68 (40.7)	26 (25.2)	12 (15.8)

Joint range-of-motion				
Ankle joint dorsiflexion - knee extended, degrees ^a	62.4 (61.6, 63.2)	63.5 (62.2, 64.8)	63.1 (61.5, 64.8)	63.1 (61.4, 64.9)
Ankle joint dorsiflexion - knee flexed, degrees ^a	52.4 (51.6, 53.1)	54.4 (53.1, 55.7)	50.8 (49.2, 52.5)	54.9 (53.0, 56.8)
Subtalar inversion, degrees	27.4 (26.8, 28.1)	25.1 (24.0, 26.3)	27.7 (26.2, 29.2)	23.7 (21.8, 25.6)
Subtalar eversion, degrees	11.8 (11.3, 12.3)	10.8 (10.0, 11.7)	12.2 (11.1, 13.3)	11.9 (10.3, 13.4)
First MTPJ dorsiflexion, degrees	66.9 (65.4, 68.3)	63.2 (60.6, 65.8)	60.0 (56.3, 63.6)	59.4 (55.0, 63.8)

Values are presented as mean (95% CI) unless otherwise noted.

TNJ: talonavicular joint; NCJ: navicular-cuneiform joint; CMJ: cuneiform-metatarsal joint; OA: osteoarthritis; BMI: body mass index; MFPDI: Manchester Foot Pain & Disability Index; NRS: numerical rating scale; MTPJ: metatarsophalangeal joint

^a Lower values indicate greater range of motion

Table 2. Relationship between midfoot OA groups and clinical foot and ankle characteristics (outcomes), adjusted for age, sex, BMI and presence of 1st MTPJ OA.

	Medial midfoot OA (n=168) TNJ or NCJ or 1 st CMJ (& no 2 nd CMJ)		Central midfoot OA (n=103) 2 nd CMJ only		Combined medial & central midfoot OA (n=76) TNJ or NCJ or 1 st CMJ & 2 nd CMJ	
	Adjusted OR	95% CI	Adjusted OR	95% CI	Adjusted OR	95% CI
Foot pain and deformity						
Dorsal midfoot pain	1.54	1.02, 2.33	1.59	0.95, 2.66	2.54	1.45, 4.44
Plantar midfoot pain	0.95	0.69, 1.31	0.88	0.53, 1.45	0.63	0.37, 1.06
Midfoot bony exostosis	1.29	0.90, 1.85	1.14	0.69, 1.87	1.29	0.78, 2.15
Hallux valgus (Y/N)	1.18	0.79, 1.75	1.04	0.60, 1.80	1.76	1.02, 3.05
	Adjusted β	95% CI	Adjusted β	95% CI	Adjusted β	95% CI
Foot pain severity in last month	0.001	-0.001, 0.003	0.000	-0.002, 0.003	0.002	-0.001, 0.005
MFPDI Pain Score	0.000	-0.002, 0.003	0.004	0.0002, 0.008	0.004	0.0000002, 0.008
MFPDI Function Score	0.001	-0.001, 0.002	0.001	-0.001, 0.003	0.002	-0.0003, 0.005
Foot posture						
Foot Posture Index	-0.08	-0.33, -0.16	0.19	-0.12, 0.51	0.44	0.12, 0.77
Arch Index	0.005	-0.002, 0.01	0.01	0.000001, 0.02	0.02	0.01, 0.03
Navicular height	-0.002	-0.006, 0.003	-0.006	-0.01, 0.001	-0.01	-0.01, -0.00
Joint range-of-motion						
Ankle joint dorsiflexion - knee extended, degrees	0.59	-0.54, 1.74	-0.60	-2.12, 0.90	-1.00	-2.76, 0.75
Ankle joint dorsiflexion - knee flexed, degrees	1.11	-0.12, 2.35	-1.46	-2.92, -0.005	-0.54	-2.57, 1.49
Subtalar inversion, degrees	-1.71	-2.95, -0.47	0.51	-1.40, 2.42	-2.45	-4.41, -0.48
Subtalar eversion, degrees	-0.34	-1.35, 0.67	0.91	-0.56, 2.39	0.55	-1.02, 2.13
First MTPJ dorsiflexion, degrees	-1.71	-3.96, 0.54	-2.06	-5.10, 0.97	-4.30	-8.38, -0.21

Odds ratios (95% confidence intervals) are presented for binary outcome variables. Beta coefficients with 95% confidence intervals are presented for continuous variables. No or minimal midfoot OA is the reference category. Bold text indicates the result is considered statistically significant (odds ratio does not cross one or beta coefficient does not cross zero).

TNJ: talonavicular joint; NCJ: navicular-cuneiform joint; CMJ: cuneiform-metatarsal joint; OA: osteoarthritis; MFPDI: Manchester Foot Pain and Disability Index. MTPJ: metatarsophalangeal joint; CI: confidence interval