

Marshall Michelle (Orcid ID: 0000-0001-8163-6948)  
Thomas Martin J (Orcid ID: 0000-0002-4951-9925)  
Menz Hylton B (Orcid ID: 0000-0002-2045-3846)  
Roddy Edward (Orcid ID: 0000-0002-8954-7082)

Running header: Long-term trajectories of foot pain

**Identifying long-term trajectories of foot pain severity and potential prognostic factors:  
a population-based cohort study**

**Michelle Marshall PhD<sup>1</sup>, Milica Blagojevic-Bucknall PhD<sup>1</sup>, Trishna Rathod-Mistry PhD<sup>1</sup>,  
Martin J Thomas PhD<sup>1,2</sup>, John J Edwards PhD<sup>1</sup>, George Peat PhD<sup>1</sup>, Hylton B Menz DSc<sup>1,3</sup>,  
Edward Roddy DM<sup>1,2</sup>**

<sup>1</sup> Primary Care Centre Versus Arthritis, School of Medicine, Keele University, Staffordshire,  
ST5 5BG, United Kingdom

<sup>2</sup> Haywood Academic Rheumatology Centre, Midlands Partnership NHS Foundation Trust,  
Haywood Hospital, Burslem, Staffordshire, ST6 7AG, United Kingdom

<sup>3</sup> School of Allied Health, Human Services and Sport, College of Science, Health and  
Engineering, La Trobe University, Melbourne, Victoria 3086, Australia

**Corresponding author:** Michelle Marshall; Primary Care Centre Versus Arthritis, School of  
Medicine, Keele University, Staffordshire, ST5 5BG, United Kingdom;  
[m.marshall@keele.ac.uk](mailto:m.marshall@keele.ac.uk); Tel no: 0044 1782 734872

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## ABSTRACT

**Objectives:** To identify distinct foot pain trajectories over seven years and examine their associations with potential prognostic factors.

**Methods:** Adults aged  $\geq 50$  years registered with four general practices in North Staffordshire, UK were mailed a baseline health survey. Those reporting current or recent foot pain were invited to attend a research assessment clinic. Follow-up was by repeated postal surveys at 18, 36, 54, and 84 months. Distinct trajectories of foot pain were explored using Latent Class Growth Analysis (LCGA). Subsequently, identified trajectories were combined into most and least progressive groups and covariate-adjusted associations with a range of prognostic factors examined.

**Results:** Of 560 adults with foot pain attending baseline research clinics, 425 (76%) provided data at baseline and  $\geq 2$  follow-up time-points. LCGA for foot pain severity (0-10 Numerical Rating Scale) identified a four-trajectory model: 'mild, improving' (37%); 'moderate, improving' (33%); 'moderate-severe, persistent' (24%); 'severe, persistent' (6%). Compared with individuals in more favourable ('improving') pain trajectories, those in less favourable ('persistent') pain trajectories were more likely to be obese, have routine/manual and intermediate occupations, poorer physical and mental health, catastrophising beliefs, greater foot-specific functional limitation, and self-assessed hallux valgus at baseline.

**Conclusions:** Four distinct trajectories of foot pain were identified over a seven-year period, with one-third of individuals classified as having pain that is persistently moderate-severe and severe in intensity. The effect of intervening to target modifiable prognostic factors such as obesity and hallux valgus on long-term outcomes in people with foot pain requires investigation.

**Significance and Innovation:**

- Individuals with joint pain often believe their pain will get worse over time but there are few prospective studies of foot pain and OA.
- Over seven years, one-third of individuals had persistent moderate-severe or severe foot pain. Reassurance is provided that many people with foot pain improve over time.
- Persistent pain was associated with obesity, routine/manual and intermediate occupations, poorer physical and mental health, catastrophising beliefs, foot-specific functional limitation, and hallux valgus at baseline.
- Future research should investigate if targeting modifiable prognostic factors such as obesity and hallux valgus improves long-term outcomes in people with foot pain.

## INTRODUCTION

Foot pain affects 24% of adults aged 45 years and over and accounts for 8% of primary care musculoskeletal consultations in the UK.[1-2] Painful foot disorders are major causes of restricted activity, poor balance and risk of falling, particularly in older people.[1,3] Symptomatic osteoarthritis (OA) is the leading global cause of years lived with disability in older people,[4] and is likely to be a significant contributor to foot pain in this age group.[5]

Few prospective studies of foot pain and OA have been undertaken and little is known about what happens to people over time. Longitudinal studies of foot OA to date have focused on radiographic progression, rather than change in symptoms, finding that structural progression after 3 and 19 years occurred in only a third of people.[6-7] At other joint sites including the knee, hip and hand, distinct pain trajectories and specific generic and joint-specific risk factors for pain progression have been identified, showing that OA symptoms fluctuate over time and vary greatly between individuals.[8-12]

Better understanding of the prognosis and natural history of foot pain is needed to develop a coherent clinical approach to helping people with painful foot OA and strategies to reduce the impact of related pain and disability in older people. This information could also help identify where treatment need is greatest, whether there are modifiable risk factors that could be targeted, and to inform intervention development for future clinical trials.

The objectives of this study were to identify distinct trajectories of foot pain and function over seven years in community-dwelling individuals aged 50 years and over and examine associations between trajectories and potential prognostic factors.

## **PATIENTS AND METHODS**

### **Study population and data collection**

This was a prospective observational cohort study, the Clinical Assessment Study of the Foot (CASF).[13] Ethical approval was obtained at baseline, 18, 36 and 54 month follow-up from Coventry Research Ethics Committee (REC project number: 10/H1210/5) and at 84 month follow-up from East Midlands – Leicester South Research Ethics Committee (REC project number: 18/EM/0249).

At baseline (May 2010-July 2011), a postal health survey was sent to community-dwelling adults aged  $\geq 50$  years registered with four general practices in North Staffordshire, UK. The health survey collected information on: foot pain severity (0-10 numerical rating scale (NRS));[14] foot pain and foot-specific function (Manchester Foot Pain and Disability Index (MFPDI));[15] self-reported hallux valgus using a validated line drawing instrument where the three most severe grades (representing 30, 45 and 60 degrees of angulation) indicate presence of the condition;[16] general health (Short Form-12 (SF-12));[17] anxiety and depression (Hospital Anxiety and Depression Scale (HADS));[18] coping strategies;[19] and demographic and socioeconomic characteristics. Participants provided written informed consent to participate and to further contact in the postal questionnaire.

Individuals who reported experiencing foot pain within the preceding 12 months at baseline and provided consent to further contact were invited to attend a research clinic where assessments were undertaken including the Foot Posture Index (FPI)[20] and height and weight were measured. Weight-bearing dorso-plantar and lateral radiographs of each foot were obtained. Osteophytes and joint space narrowing were graded separately in the 1st metatarsophalangeal joint (MTPJ), 1st and 2nd cuneometatarsal joints (CMJs), navicular-first cuneiform joint (NCJ) and talonavicular joint (TNJ) using a 0-3 scale according to a standardised foot atlas.[21] Radiographic OA was defined as grade  $\geq 2$  for either feature on either view in one or more joints. Symptomatic radiographic foot OA phenotypes (no/minimal foot OA, isolated first MTP joint OA, polyarticular foot OA) were defined as described previously.[22] Further written informed consent was obtained to undergo assessment at the research clinic.

Participants' consent for review of their medical records was requested. Participants with gout were identified from the primary care medical records, and inflammatory arthritis (non-specific inflammatory arthritis, rheumatoid arthritis or psoriatic arthritis) were identified from the primary care and hospital medical records and a clinical x-ray report by a consultant musculoskeletal radiologist.

All baseline clinic attenders received follow-up postal health surveys at 18, 36, 54, and 84 months, other than deceased participants and those who had revoked consent or whose general practitioner had deemed inappropriate to contact. At each time-point, survey content was similar to baseline and non-responders were sent reminders two and four weeks after mailing, followed by attempts to collect key outcomes (MFPDI function

subscale, global assessment of change, and pain, aching and stiffness in previous month) by telephone and post.

### **Outcomes**

The main outcome was foot pain severity in the previous month (0-10 NRS) completed at each of the five time-points.[14] The impact of foot pain and function were also assessed at all time-points using the MFPDI pain and functional limitation subscales.[15] These subscales fit the Rasch model allowing interval-level data to be generated. Higher Rasch-transformed scores indicate greater pain and limitation.[23]

### **Public and patient involvement**

People with foot pain contributed to study design, conduct and dissemination. They prioritised pain and impaired function as the most important outcomes and informed questionnaire content. Individuals assisted with baseline clinical assessment training, refining the assessment protocol. They contributed to interpretation of findings and dissemination plans.

### **Statistical analysis**

Latent class growth analysis (LCGA) was used to model repeated measures of foot pain (0-10 NRS) at five time-points over 84 months. For inclusion in the analysis, participants were required to have foot pain data at baseline and  $\geq 2$  of the four follow-up time-points. The optimal number of trajectories was selected using a combination of statistical, parsimony and interpretability criteria.[24]



Three models were tested initially, with solely linear, quadratic or cubic specifications for trajectories. In each case, the number of modelled trajectories was increased and significance of the improvement in the model fit assessed using Akaike information criterion (AIC), Bayesian Information Criterion (BIC) and sample size adjusted (SSA-BIC) (smaller values indicating better fit). The Lo, Mendell and Rubin (LMR) adjusted likelihood ratio test (LRT),<sup>[25]</sup> and the bootstrap LRT were used to assess whether there was a significant improvement in model fit between  $k-1$  and  $k$  trajectory models. Additionally, the following criteria were used for model selection: (1) delineation of trajectories assessed by higher entropy (range 0-1), (2) clear classification of participants into trajectories (average posterior probability  $>0.7$ ,<sup>[26]</sup> (3) trajectory membership  $\geq 4\%$  of the study population, and (4) clinical relevance and interpretation of the identified trajectories.<sup>[24]</sup> Mixed polynomial models were derived allowing the specification for trajectories to differ. An appropriate polynomial functional form for each trajectory was chosen, based on the significance of the estimated parameters related to each polynomial component,<sup>[26]</sup> with each participant assigned to the most appropriate trajectory using the maximum probability assignment principle. Improvement of model fit with each additional trajectory was then assessed.

We assessed sensitivity of our findings by modifying various components of our analyses. A complete case analysis of those with foot pain severity data at all five time-points was undertaken to examine whether trajectories could be replicated. We also examined whether similar trajectories could be identified using the MFPDI pain and functional limitation subscales. LCGA assumes that individual participant patterns within a particular trajectory are homogeneous. We relaxed this assumption and allowed growth parameters

to vary within trajectories by applying a growth mixture model (GMM), of which LCGA is a subclass. For all LCGA and GMM models, full information maximum likelihood estimation with robust standard errors was employed, and to avoid convergence at local maxima, each model was fitted using 1000 random sets of starting values and 50 final stage optimisations carried out for each.

A nested case-control study was undertaken to compare those in the most progressive (cases) and least progressive trajectories (controls) of the final selected model. Crude univariable associations between progression and baseline characteristics including sociodemographic (age, sex, body mass index (BMI), attended higher education, occupational class), general and mental health (SF12, HADS, catastrophising beliefs) and foot-specific characteristics (FPI, MFPDI, presence of hallux valgus, radiographic OA phenotype) (odds ratios (OR) and 95% confidence intervals (CI)) were assessed using logistic regression models and subsequently adjusted for age, sex and BMI as potential confounders of OA severity. Additionally, the relationship between the most progressive and least progressive foot pain NRS trajectories and the MFPDI function sub-scale at 7 years was examined adjusted for baseline score, age, sex and BMI.

The GRoLTS checklist for reporting latent trajectory studies was followed.[27] Statistical significance was assumed at  $p$ -value $<0.05$ . Analyses were performed in STATA (v15.0 StataCorp LLC, Texas, USA) and Mplus (v8.0).[28]

## RESULTS

560 participants who reported having foot pain in the last 12 months and consented to further contact attended the baseline research assessment clinic. Follow-up data were received from 501 participants (89%) at 18 months, 455 (81%) at 36 months, 356 (64%) at 54 months and 309 (55%) at 84 months. 425 (76%) participants had pain NRS data at baseline and  $\geq 2$  follow-up time-points. These participants were younger (mean age 64.4 vs 66.8 years), less likely to be female (52.7 vs 65.9%), had significantly lower foot pain NRS (mean 5.2 vs 5.8), and SF-36 score (mean 30.1 vs 32.0) at baseline than the remaining participants who had data at baseline but  $< 2$  follow-up time-points.

Three hundred and ninety-six participants (94.3%) reported foot pain in the last month; over half reported having foot pain, aching or stiffness on most or all days (Table 1). Nearly two-thirds had radiographic foot OA affecting one or more foot joints, 44.5% had self-reported hallux valgus, and only 3.5% had gout and 4.0% inflammatory arthritis. Concomitant foot conditions were common (32.2%,  $n=137$ ).

A four trajectory model was selected as optimal based on low AIC, BIC and SSA-BIC values, significance of bootstrap LRT, while maintaining high entropy and average posterior probabilities (Supplementary Table 1). Additionally, this model identified a small but clinically important subgroup of patients reporting high pain severity.

The four identified trajectories were labelled as 'mild, improving pain' ( $n=156$ , 36.7%), 'moderate, improving pain' ( $n=139$ , 32.7%), 'moderate-severe, persistent pain' ( $n=104$ , 24.5%) and 'severe, persistent pain' ( $n=26$ , 6.1%). Individuals in the mild improving pain trajectory had a mean NRS pain severity score of 3.6 at baseline which improved over 18

months and was sustained over follow-up (slope parameter estimate=-3.513,  $p<0.001$ ) (Figure 1). Those in the moderate improving pain trajectory had a mean pain score of 5.1 at baseline which steadily declined over follow-up (slope parameter estimate=-0.489,  $p<0.001$ ). The moderate-severe persistent pain trajectory had a mean pain score of 6.7 at baseline which was sustained over follow-up (slope parameter estimate=-0.138,  $p=0.321$ ). Finally, those in the severe persistent pain trajectory had a mean pain score of 8.4 at baseline with consistently high levels of pain over follow-up (slope parameter estimate=0.037,  $p=0.787$ ). Figure 2 depicts individual observed growth trajectories within each trajectory and Table 1 displays the baseline characteristic for each of the four trajectories.

Comparable trajectories for NRS foot pain severity were obtained on complete case analysis ( $n=273$ , Supplementary Figure 1). Similar trajectories were also identified for the MFPDI pain ( $n=379$ ), and functional limitation ( $n=384$ ) subscales scores (Supplementary Figures 2 and 3). On fitting a GMM, an optimal model with fewer trajectories (three) was identified than via LCGA (Supplementary Table 2), however this was expected since GMM allows for within-trajectory growth variation. It was possible to replicate the four-trajectory model, however the severe persistent category consisted of <4% participants.

Baseline characteristics of individuals in moderate-severe and severe persistent foot pain severity trajectories ( $n=130$ , 30.6%) were compared to those in mild and moderate improving trajectories ( $n=295$ , 69.4%) (Table 2). On adjustment, the less favourable long-term foot pain NRS trajectories were significantly associated with higher BMI (aOR 1.06 95%CI 1.02 to 1.11), intermediate occupations 2.69 (1.39 to 5.21) and routine and manual occupation 2.01 (1.15 to 3.53) vs managerial and professional occupations, worse MFPDI

foot pain (2.19 [1.80 to 2.66]) and functional limitation (1.78 [1.54 to 2.05]), hallux valgus in either foot (2.22 [1.43 to 3.44]), poorer physical (0.93 [0.91 to 0.95]) and mental health (0.95 [0.93 to 0.97]), greater anxiety (1.15 [1.09 to 1.21]) and depression (1.21 [1.14 to 1.29]), and catastrophising beliefs (1.36 [1.23 to 1.50]). Less favourable trajectories were not significantly associated with the presence of radiographic foot OA phenotype (1<sup>st</sup> MTPJ OA 1.21 [0.70 to 2.08], polyarticular OA 1.38 [0.74 to 2.54] vs no/minimal OA).

Moderate-severe and severe persistent foot pain NRS trajectories over 7 years were also accompanied by greater foot-specific functional limitation (MPDI function subscale) at 7 years (aOR=1.43 [95%CI 1.16, 1.76]) after adjustment for baseline score, age, sex and BMI compared to those with mild and moderate improving pain trajectories.

## DISCUSSION

In community-dwelling individuals aged 50 years and over with foot pain, we identified four distinct trajectories of foot pain severity over seven years: mild improving, moderate improving, moderate-severe persistent and severe persistent pain. Individuals in the less favourable moderate-severe and severe persistent pain trajectories were more likely at baseline to be obese; have greater foot-specific functional limitation, hallux valgus in either foot, routine/manual and intermediate occupations, and poorer physical health and mental health; and to catastrophise about their foot pain symptoms, compared with those in the mild and moderate improving trajectories.

Our analysis shows that foot pain does not persist at the same intensity or progress in all individuals. Approximately one-third of the people who reported foot pain in the last year at baseline had persistent pain over seven years, and there was a small but important group where pain was persistently severe. This group consisted of 6% of the study population and the majority (69.2%; 18/26) had radiographic OA, two of which had concomitant gout and one person had inflammatory arthritis. On average people in this 'severe, persistent' pain trajectory reported pain of 8-9/10 at each time point, a pain level which they are likely to consider as being unmanageable.[29] In a previous community-based study from the same geographic area, foot pain was found to persist over three years in more than two-thirds of participants,[30] however, persistence was defined by presence rather than severity of pain.

Although to our knowledge foot symptom trajectories have not previously been investigated, symptom trajectories at other sites including the knee and hip have been explored.[8-12,31-38] Studies of symptom trajectories are heterogeneous, varying by length (18 months to 14 years) and frequency (3 months to 2 years) of follow-up,[8,32-33] sample size (222 to 4796),[8,34] and how OA was defined,[8-11,32,34] as well as age and sex characteristics of the study populations. Despite these variations, these studies found pain trajectories similar in number (between three and six) and pattern.[35] Trajectories are often stable with a similar level of symptoms over time but at different thresholds (e.g. mild, moderate and severe).[9-11,31,34-35] We found also improving pain trajectories which have been similarly been reported at the knee and hip.[8,12,36-38] However, we did not identify a group of people with highly progressive pain noted in several previous pain severity studies.[8,12,37] While rapidly progressing forms of hip and

knee OA have been established,[39-40] our results provide no indication that this occurs at the foot. Structural progression of radiographic 1<sup>st</sup> MTPJ OA has been reported over three and 19 years in approximately a third of participants in two prospective cohorts.[6-7] However, as symptoms and radiographic change are often discordant, it cannot be assumed that the individuals with persistent pain in our study also have structural progression.

Obesity, routine/manual and intermediate occupations, foot-specific functional limitation, poorer physical and mental health and hallux valgus have previously been found to associate with foot pain in cross-sectional studies,[41-44] but few have been examined longitudinally. BMI has been found to be a predictor of future foot pain and an increase in BMI associated with an increase in foot pain over two years [45-46] and its persistence over six years.[47] Worsening hallux valgus severity has been associated with greater foot pain over six years.[48-49] Depression has been found to be a predictor of future foot pain and poorer mental health associated with worsening of foot pain over three years.[45,50] While not examined previously at the foot, having poorer general health, poorer coping strategies and occupation have been reported to be associated with poorer hip and knee pain trajectories.[9,12,36]

Pain has previously been found to be associated with increased risk of functional impairment development and progression, with stronger associations found for increased pain severity.[51-53] The mechanisms underlying the association between pain and functional decline are not fully understood, but it is thought that individuals with joint pain often become less active often to avoid the pain and/or believe that they could make

their condition worse.[54] It is also believed that pain can reduce joint range of motion.[55] In the long term, both these pathways are considered to result in deterioration of physical performance and muscle weakness, which gradually leads to functional impairment and disability.[56]

Strengths of this study include a prospective cohort design in a community-dwelling population not selected based on primary care consultation or referral. It is the first study to examine trajectories of foot pain prospectively over several follow-up time-points. The quality of classification of the four-trajectory model was high, as judged by the average posterior probabilities and entropy value. The model was robust to missing data and model assumptions. Furthermore, similar trajectories were replicated in the complete case analysis, despite evidence of attrition bias, and for other foot outcomes.

A number of limitations should also be acknowledged. The source study population, the CASF study, has low representation of ethnic minorities.[13]. Pain severity was collected at the person-level and so included both feet. It is therefore possible that the specific foot or regions of the foot with the most severe pain varied over time. Incident cases of foot pain \*were not specifically examined, and it is possible that the different trajectories may represent different stages of foot disease. Individuals with OA commonly report fluctuations and flares in their symptoms, and it is unknown how these short-term changes are reflected in the trajectories as the interval between data collection points was fairly long.[57-58] Equidistance between follow-up time points was assumed in the analysis, which was the case for 4 out of 5 time points. The time-period between the penultimate and last time points was 6 months longer, but this is unlikely to have had an



effect on the results over 7 years. It is unknown to what extent clinical treatment and self-management influenced the trajectories identified. However, previous studies suggest that only a minority of individuals with foot pain consult primary care, with most prescribed analgesics, and few receiving onward treatment referrals.[59-60] Additionally, some of the baseline characteristics in the nested case control analysis, such as the symptomatic radiographic phenotypes, were less prevalent than anticipated leading to insufficient power and a type II error.

Our study has important implications for individuals with foot pain, clinicians and policy makers. Individuals with joint pain often believe that it is inevitable that their pain will get worse over time,[61-62] however our findings provide reassurance that not all foot pain is progressive and many people will experience some improvement over time. Our findings will aid identification of individuals with moderate and severe persistent pain at risk of worse outcomes who could be targeted for intervention. Hallux valgus and obesity were associated with progressive pain trajectories and each are potentially modifiable with orthoses and corrective surgery for hallux valgus and with diet and exercise for obesity.[63-65] There is a need for well-designed intervention studies to determine if individuals with different trajectories would benefit from early intervention and whether specific interventions for hallux valgus and obesity influence foot symptoms.

In conclusion, over a seven-year period, one-third of individuals had persistent moderate to severe or severe pain, that was accompanied by a decline in foot-specific function. Obesity and hallux valgus have been identified as possible prognostic factors. Further investigation to

ascertain whether interventions targeting these factors improve long-term outcomes in people with foot pain are warranted.

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**Ethics approval:**

Baseline, 18, 36 and 54 month follow-up was approved by Coventry Research Ethics Committee (REC project number: 10/H1210/5) and 84 month follow-up was approved by East Midlands – Leicester South Research Ethics Committee (REC project number: 18/EM/0249).

## References

1. Thomas MJ, Roddy E, Zhang W, Menz HB, Hannan MT, Peat GM. The population prevalence of foot and ankle pain in middle and old age: a systematic review. *Pain* 2011;152:2870–80.
2. Menz HB, Jordan KP, Roddy E, Croft PR. Characteristics of primary care consultations for musculoskeletal foot and ankle problems in the UK. *Rheumatol* 2010;49:1391-8.
3. Menz HB, Auhl M, Spink MJ. Foot problems as a risk factor for falls in community-dwelling older people: A systematic review and meta-analysis. *Maturitas* 2018;118:7-14.
4. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2163-96.
5. Roddy E, Menz HB. Foot osteoarthritis: latest evidence and developments. *Ther Adv Musculoskelet Dis* 2018; 10:91-103.
6. Wilder FV, Barrett JP Jr, Farina EJ. Effect of regular exercise on the radiographic progression of foot osteoarthritis. *J Am Podiatr Med Assoc* 2005;95:342-6.
7. Bowen C, Gates L, McQueen P, Daniels M, Delmestri A, Drechsler W, et al. The natural history of radiographic first metatarsophalangeal joint osteoarthritis: a nineteen-year population based cohort study. *Arthritis Care Res (Hoboken)* 2020;72:1224-30.
8. Verkleij SP, Hoekstra T, Rozendaal RM, Waarsing JH, Koes BW, Luijsterburg PA, et al. Defining discriminative pain trajectories in hip osteoarthritis over a 2-year time period. *Ann Rheum Dis* 2012;71:1517-23.

9. Nicholls E, Thomas E, van der Windt DA, Croft PR, Peat G. Pain trajectory groups in persons with, or at high risk of, knee osteoarthritis: findings from the Knee Clinical Assessment Study and the Osteoarthritis Initiative. *Osteoarthritis Cartilage* 2014;22:2041-50.
10. Holla JF, van der Leeden M, Heymans MW, Roorda LD, Bierma-Zeinstra SM, Boers M, et al. Three trajectories of activity limitations in early symptomatic knee osteoarthritis: a 5-year follow-up study. *Ann Rheum Dis* 2014;73:1369-75.
11. Collins JE, Katz JN, Dervan EE, Losina E. Trajectories and risk profiles of pain in persons with radiographic, symptomatic knee osteoarthritis: data from the osteoarthritis initiative. *Osteoarthritis Cartilage* 2014;22:622-30.
12. Bastick AN, Verkleij SP, Damen J, Wesseling J, Hilberdink WK, Bindels PJ, et al. Defining hip pain trajectories in early symptomatic hip osteoarthritis--5 year results from a nationwide prospective cohort study (CHECK). *Osteoarthritis Cartilage* 2016;24:768-75.
13. Roddy E, Thomas MJ, Marshall M, Rathod T, Myers H, Menz HB, et al. The population prevalence of symptomatic radiographic foot osteoarthritis in community-dwelling older adults: cross-sectional findings from the clinical assessment study of the foot. *Ann Rheum Dis* 2015;74:156-63.
14. Williamson A & Hoggart B. Pain: a review of three commonly used pain rating scales. *J Clin Nurs* 2005;14:798-804
15. Garrow AP, Papageorgiou AC, Silman AJ, Thomas E, Jayson MI, Macfarlane GJ. Development and validation of a questionnaire to assess disabling foot pain. *Pain* 2000;85:107-13.
16. Roddy E, Zhang W, Doherty M. Validation of a self-report instrument for assessment of hallux valgus. *Osteoarthritis Cartilage* 2007;15:1008-12.

17. Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220-33.
18. Zigmond AS & Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361-70.
19. Jensen MP, Keefe FJ, Lefebvre JC, Romano JM, Turner JA. One- and two-item measures of pain beliefs and coping strategies. *Pain* 2003;104:453-69.
20. Redmond AC, Crosbie J, Ouvrier RA. Development and validation of a novel rating system for scoring standing foot posture: the Foot Posture Index. *Clin Biomech (Bristol, Avon)* 2006;21:89-98.
21. Menz HB, Munteanu SE, Landorf KB, Zammit GV, Cicutini FM. Radiographic classification of osteoarthritis in commonly affected joints of the foot. *Osteoarthritis Cartilage* 2007;15:1333-8.
22. Rathod T, Marshall M, Thomas MJ, Menz HB, Myers HL, Thomas E, et al. Investigations of Potential Phenotypes of Foot Osteoarthritis: Cross-Sectional Analysis From the Clinical Assessment Study of the Foot. *Arthritis Care Res (Hoboken)* 2016;68:217-27
23. Muller S, Roddy E. A rasch analysis of the Manchester foot pain and disability index. *J Foot Ankle Res* 2009;2:29.
24. Jung T, Wickrama KAS. An introduction to latent class growth analysis and growth mixture modeling. *Social and Personality Psychology Compass* 2008;2:302-17.
25. Lo Y, Mendell NR, Rubin DB. Testing the number of components in a normal mixture. *Biometrika* 2001;88:767-78.
26. Andruff H, Carraro N, Thompson A, Gaudreau P. Latent Class Growth Modelling: a tutorial. *Tutorials in Quantitative Methods for Psychology* 2009;5:11-24.

27. van de Schoot R, Sijbrandij M, Winter SD, Depaoli S, Vermunt JK. The GROLTS-checklist: guidelines for reporting on latent trajectory studies. *Struct. Equation Model* 2017;24:451–67.
28. Muthén LK, Muthén BO. Mplus User's Guide. Eighth Edition. Los Angeles, CA: Muthén & Muthén (1998-2017).
29. Zelman DC, Hoffman DL, Seifeldin R, Dukes EM. Development of a metric for a day of manageable pain control: derivation of pain severity cut-points for low back pain and osteoarthritis. *Pain* 2003;106:35-42.
30. Roddy E, Muller S, Thomas E. Onset and persistence of disabling foot pain in community-dwelling older adults over a 3-year period: a prospective cohort study. *J Gerontol A Biol Sci Med Sci* 2011;66:474-80.
31. Leffondré K, Abrahamowicz M, Regeasse A, Hawker GA, Badley EM, McCusker J, et al. Statistical measures were proposed for identifying longitudinal patterns of change in quantitative health indicators. *J Clin Epidemiol* 2004;57:1049-62.
32. Hermsen LA, Smalbrugge M, van der Wouden JC, Leone SS, Dekker J, van der Horst HE. Trajectories of physical functioning and their prognostic indicators: a prospective cohort study in older adults with joint pain and comorbidity. *Maturitas* 2014;78:316-22.
33. James RJE, Walsh DA, Ferguson E. Trajectories of pain predict disabilities affecting daily living in arthritis. *Br J Health Psychol* 2019;24:485-96.
34. Dai Z, Lu N, Niu J, Felson DT, Zhang Y. Dietary Fiber Intake in Relation to Knee Pain Trajectory. *Arthritis Care Res (Hoboken)* 2017;69:1331-9.

35. Wieczorek M, Rotonda C, Guillemin F, Rat AC. What have we learned from trajectory analysis of clinical outcomes in knee and hip osteoarthritis before surgery? *Arthritis Care Res (Hoboken)* 2019 Sep 17. [Epub ahead of print]. doi: 10.1002/acr.24069.
36. Wesseling J, Bastick AN, ten Wolde S, Kloppenburg M, lafeber FPJG, Bierma-Zeinstra SMA, et al. Identifying Trajectories of Pain Severity in Early Symptomatic Knee Osteoarthritis: A 5-year Follow up of the Cohort Hip and Cohort Knee (CHECK) Study. *J Rheumatol* 2015;42:1470-7.
37. Bastick AN, Wesseling J, Damen J, Verkleij SP, Emans PJ, Bindels PJ, et al. Defining knee pain trajectories in early symptomatic knee osteoarthritis in primary care: 5-year results from a nationwide prospective cohort study (CHECK). *Br J Gen Pract* 2016;66:e32-9.
38. Schiphof D, Runhaar J, Waarsing JH, van Spil WE, van Middelkoop M, Bierma-Zeinstra SMA. The clinical and radiographic course of early knee and hip osteoarthritis over 10 years in CHECK (Cohort Hip and Cohort Knee). *Osteoarthritis Cartilage* 2019;27:1491-1500.
39. Davis J, Eaton CB, Lo GH, Lu B, Price LL, McAlindon TE, et al. Knee symptoms among adults at risk for accelerated knee osteoarthritis: data from the Osteoarthritis Initiative. *Clin Rheumatol* 2017;36:1083-9.
40. Flemming DJ, Gustas-French CN. Rapidly Progressive Osteoarthritis: a Review of the Clinical and Radiologic Presentation. *Curr Rheumatol Rep* 2017;19:42.
41. Butterworth PA, Landorf KB, Smith SE, Menz HB. The association between body mass index and musculoskeletal foot disorders: a systematic review. *Obes Rev* 2012;13:630-42.

42. Hill CL, Gill TK, Menz HB, Taylor AW. Prevalence and correlates of foot pain in a population-based study: the North West Adelaide health study. *J Foot Ankle Res* 2008;1:2.
43. Hendry GJ, Fenocchi L, Woodburn J, Steultjens M. Foot pain and foot health in an educated population of adults: results from the Glasgow Caledonian University Alumni Foot Health Survey. *J Foot Ankle Res* 2018;11:48.
44. Laslett LL, Menz HB, Otahal P, Pan F, Cicuttini FM, Jones G. Factors associated with prevalent and incident foot pain: data from the Tasmanian Older Adult Cohort Study. *Maturitas* 2018;118:38-43.
45. Gill TK, Menz HB, Landorf KB, Arnold JB, Taylor AW, Hill CL. Predictors of foot pain in the community: the North West Adelaide health study. *J Foot Ankle Res* 2016;9:23.
46. Walsh TP, Butterworth PA, Urquhart DM, Cicuttini FM, Landorf KB, Wluka AE, et al. Increase in body weight over a two-year period is associated with an increase in midfoot pressure and foot pain. *J Foot Ankle Res* 2017;10:31.
47. Menz HB, Barr EL, Brown WJ. Predictors and persistence of foot problems in women aged 70 years and over: a prospective study. *Maturitas* 2011;68:83-7.
48. Koo KK, Tse LF, Cheng HS, Ho KKW. The progression of hallux valgus in the oriental Chinese population in Hong Kong. *Foot (Edinb)*. 2017;32:15-21.
49. Menz HB, Roddy E, Thomas E, Croft PR. Impact of hallux valgus severity on general and foot-specific health-related quality of life. *Arthritis Care Res (Hoboken)* 2011;63:396-404.
50. Butterworth PA, Urquhart DM, Cicuttini FM, Menz HB, Strauss BJ, Proietto J, et al. Relationship between mental health and foot pain. *Arthritis Care Res (Hoboken)* 2014;66:1241-5.



51. Castellanos-Perilla N, Borda MG, Fernández-Quilez Á, Aarsland V, Soennesyn H, Cano-Gutiérrez CA. Factors associated with functional loss among community-dwelling Mexican older adults. *Biomedica* 2020;40:546-56.
52. Landi F, Russo A, Liperoti R, Danese P, Maiorana E, Pahor M et al. Daily pain and functional decline among old adults living in the community. *Journal of pain and symptom management* 2009;38:350-7.
53. Leveille SG, Ling S, Hochberg MC, Resnick HE, Bandeen-Roche KJ, Won A et al. *Widespread musculoskeletal pain and the progression of disability in older disabled women. Ann Intern Med* 2009;135:1038-46.
54. Steultjens MP, Dekker J, Bijlsma JW. Avoidance of activity and disability in patients with osteoarthritis of the knee: the mediating role of muscle strength. *Arthritis Rheum* 2002;46:1784-8.
55. Young A. Current issues in arthrogenous inhibition. *Ann Rheum Dis* 1993;52:829-34.
56. Rantanen T, Guralnik JM, Foley D, Masaki K, Leveille S, Curb JD et al. Midlife hand grip strength as a predictor of older age disability. *JAMA* 1999;281:558-60.
57. Parry E, Ogollah R, Peat G. 'Acute flare-ups' in patients with, or at high risk of, knee osteoarthritis: a daily diary study with case-crossover analysis. *Osteoarthritis Cartilage* 2019;27:1124-8.
58. Thomas MJ, Neogi T. Flare-ups of osteoarthritis: what do they mean in the short-term and the long-term? *Osteoarthritis Cartilage*. 2020;28:870-3.
59. Ferguson R, Culliford D, Prieto-Alhambra D, Pinedo-Villanueva R, Delmestri A, Arden N, et al. Encounters for foot and ankle pain in UK primary care: a population-based cohort study of CPRD data. *Br J Gen Pract* 2019;69:e422-9.

60. Paterson KL, Harrison C, Britt H, Hinman RS, Bennell KL. Management of foot/ankle osteoarthritis by Australian general practitioners: an analysis of national patient-encounter records. *Osteoarthritis Cartilage* 2018;26:888-94.
61. Sarkisian CA, Hays RD, Mangione CM. Do older adults expect to age successfully? The association between expectations regarding aging and beliefs regarding healthcare seeking among older adults. *J Am Geriatr Soc* 2002;50:1837-43.
62. Darlow B, Brown M, Thompson B, Hudson B, Grainger R, McKinlay E, et al. Living with osteoarthritis is a balancing act: an exploration of patients' beliefs about knee pain. *BMC Rheumatol* 2018;2:15.
63. Chadchavalpanichaya N, Prakotmongkol V, Polhan N, Rayothee P, Seng-lad S. Effectiveness of the custom-mold room temperature vulcanizing silicone toe separator on hallux valgus: A prospective, randomized single-blinded controlled trial. *Prosthet Orthot Int* 2018;42:163-70.
64. Abdalbary SA. Foot Mobilization and Exercise Program Combined with Toe Separator Improves Outcomes in Women with Moderate Hallux Valgus at 1-Year Follow-up: a randomised clinical trial. *J Am Podiatr Med Assoc* 2018;108:478-86.
65. Hall M, Castelein B, Wittoek R, Calders P, Van Ginckel A. Diet-induced weight loss alone or combined with exercise in overweight or obese people with knee osteoarthritis: A systematic review and meta-analysis. *Semin Arthritis Rheum* 2019;48:765-77.

**FIGURE LEGENDS**

Figure 1. Foot pain severity trajectories over seven years

Figure 2. Estimated trajectories and individual observed growth trajectories

**Table 1. Baseline characteristics of the study population and the four-trajectory model obtained by LCGA**

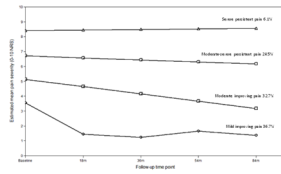
	All participants (n=425)	Mild improving pain (n=156)	Moderate improving pain (n=139)	Moderate-severe persistent pain (n=104)	Severe persistent pain (n=26)
<b>Baseline characteristics</b>					
Age, years; Mean (SD)	64.4 (7.8)	64.4 (7.3)	64.2 (8.2)	65.0 (8.1)	62.4 (7.3)
Female gender; n (%)	224 (52.7)	77 (49.4)	79 (56.8)	58 (55.8)	10 (38.5)
BMI, kg/m <sup>2</sup> ; Mean (SD)	30.2 (5.5)	29.1 (4.7)	30.4 (5.8)	31.1 (5.5)	32.5 (6.0)
Attended higher education; n (%)	114 (27.6)	51 (33.6)	37 (27.6)	18 (17.8)	8 (30.8)
Occupational class; n (%):					
Managerial and professional	111 (26.1)	55 (35.3)	35 (25.2)	19 (18.3)	2 (7.7)
Intermediate	82 (19.3)	26 (16.7)	25 (18.0)	26 (25.0)	5 (19.2)
Routine and manual	210 (49.4)	71 (45.5)	71 (51.1)	52 (50.0)	16 (61.5)
SF12 Physical component score 0-100; Mean (SD)	38.9 (12.1)	44.4 (10.2)	38.7 (12.3)	33.4 (10.8)	28.2 (8.8)
SF12 Mental component score 0-100; Mean (SD)	49.9 (10.6)	53.2 (8.5)	49.9 (10.6)	47.0 (11.2)	40.5 (10.9)
SF36 Physical functioning scale 0-100; Mean (SD)	59.6 (30.1)	75.7 (20.5)	58.8 (30.3)	44.0 (29.1)	29.2 (24.0)
HADS anxiety 0-21; Mean (SD)	6.9 (4.3)	5.7 (3.9)	6.6 (4.0)	8.1 (4.4)	10.8 (4.8)
HADS depression 0-21; Mean (SD)	5.3 (3.8)	3.9 (2.9)	5.0 (3.5)	6.6 (4.0)	9.9 (4.3)
Any foot pain, aching or stiffness in last month; n (%)	397 (93.4)	132 (84.6)	136 (97.8)	103 (99.0)	26 (100)
Any foot pain, aching or stiffness on most or all days in last month; n (%)	234 (55.1)	54 (34.6)	77 (55.4)	78 (75.0)	25 (96.2)
Foot pain severity (NRS 0-10) last month; Mean (SD)	5.2 (2.6)	3.5 (2.2)	5.4 (2.1)	6.7 (1.9)	8.6 (1.7)
MFPDI Pain subscale (Rasch); Mean (SD)	-0.21 (1.5)	-1.18 (1.4)	-0.10 (1.3)	0.62 (1.2)	1.61 (1.2)
MFPDI Function subscale (Rasch); Mean (SD)	-0.76 (2.1)	-2.02 (1.6)	-0.65 (1.9)	0.42 (1.8)	1.5 (1.8)
Foot Posture Index (Rasch); Mean (SD)					
Left foot	2.5 (1.8)	2.5 (1.7)	2.5 (1.8)	2.4 (2.0)	2.1 (2.3)
Right foot	2.5 (1.9)	2.6 (1.7)	2.5 (1.9)	2.5 (2.0)	2.3 (2.0)
Radiographic foot OA (one or more foot joints); n (%)	255 (63.7)	90 (59.6)	79 (62.2)	68 (70.1)	18 (72.0)
Symptomatic radiographic foot OA phenotypes; n (%):					
1st MTPJ OA	84 (20.7)	34 (21.8)	24 (17.3)	19 (18.3)	7 (26.9)
Polyarticular OA	62 (15.3)	14 (9.0)	25 (18.0)	21 (20.2)	2 (7.7)
Hallux valgus (either foot); n (%)	189 (44.5)	57 (36.5)	59 (42.4)	62 (59.6)	11 (42.3)
Gout; n (%)	15 (3.5)	7 (4.5)	3 (2.2)	3 (2.9)	2 (7.7)
Inflammatory arthritis (RA, PsA, other); n (%)	17 (4.0)	2 (1.3)	8 (5.8)	6 (5.8)	1 (3.8)

SD, Standard Deviation; BMI, Body Mass Index; SF12, Short-Form 12 (higher scores indicate better physical and mental health and physical function); HADS, Hospital Anxiety and Depression Scale (higher scores indicate more anxiety and depression); MFPDI, Manchester Foot Pain and Disability Index (higher scores indicate more pain and disability); MTPJ, Metatarsophalangeal Joint; RA, Rheumatoid arthritis; PsA, Psoriatic arthritis.

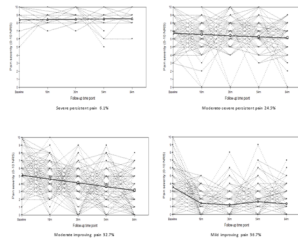
**Table 2. Baseline characteristics and their association with moderate-severe and severe persistent foot pain over seven years**

Baseline characteristics	Mild and moderate improving pain (n=295)	Moderate-severe and severe persistent pain (n=130)	Univariable Crude OR (95% CI)	Adjusted for age, sex and BMI OR (95% CI)
Age (years); Mean (SD)	64.3 (7.7)	64.5 (8.0)	1.00 (0.98, 1.03) <sup>†</sup>	1.00 (0.98, 1.03) <sup>†</sup>
Gender; n (%)				
Male	139 (46.1)	62 (47.7)	1	1
Female	156 (52.9)	68 (52.3)	0.98 (0.65, 1.48)	0.96 (0.63, 1.45)
BMI; Mean (SD)	28.1 (4.9)	29.7 (5.2)	1.06 (1.02, 1.11) <sup>†</sup>	1.06 (1.02, 1.11) <sup>†</sup>
Attended higher education; n (%)				
No	198 (67.1)	101 (77.7)	1	1
Yes	88 (29.8)	26 (20.0)	0.58 (0.35, 0.95)	0.61 (0.37, 1.01)
Occupational class; n (%):				
Managerial and professional	90 (30.5)	21 (16.2)	1	1
Intermediate	51 (17.3)	31 (23.9)	2.61 (1.36, 5.00)	2.69 (1.39, 5.21)
Routine and manual	142 (48.1)	68 (52.3)	2.05 (1.18, 3.58)	2.01 (1.15, 3.53)
Foot Posture Index (Rasch); mean (SD):				
Left foot	2.48 (1.75)	2.38 (2.07)	0.97 (0.87, 1.09) <sup>†</sup>	0.97 (0.86, 1.08) <sup>†</sup>
Right foot	2.55 (1.79)	2.48 (2.00)	0.98 (0.88, 1.10) <sup>†</sup>	0.98 (0.87, 1.10) <sup>†</sup>
Hallux valgus (either foot); n (%)				
Absence	179 (60.7)	57 (43.9)	1	1
Presence	116 (39.3)	73 (56.2)	1.98 (1.30, 3.00)	2.22 (1.43, 3.44)
MFPDI pain subscale (Rasch); mean (SD)	-0.67 (1.44)	0.82 (1.23)	2.23 (1.84, 2.70) <sup>†</sup>	2.19 (1.80, 2.66) <sup>†</sup>
MFPDI function subscale (Rasch); mean (SD)	-1.38 (1.86)	0.63 (1.84)	1.76 (1.54, 2.01) <sup>†</sup>	1.78 (1.54, 2.05) <sup>†</sup>
Radiographic foot OA phenotype; n (%):				
No/minimal OA	186 (63.1)	73 (56.2)	1	1
1st MTPJ OA	58 (19.7)	26 (20.0)	1.14 (0.67, 1.95)	1.21 (0.70, 2.08)
Polyarticular OA	39 (13.2)	23 (17.7)	1.50 (0.84, 2.69)	1.38 (0.74, 2.54)
SF12 PCS (0-100); mean (SD)	41.7 (11.60)	32.3 (10.5)	0.93 (0.91, 0.95) <sup>†</sup>	0.93 (0.91, 0.95) <sup>†</sup>
SF12 MCS (0-100); mean (SD)	51.7 (9.68)	45.6 (11.4)	0.95 (0.93, 0.97) <sup>†</sup>	0.95 (0.93, 0.97) <sup>†</sup>
HADS anxiety (0-21); mean (SD)	6.1 (3.94)	8.6 (4.58)	1.15 (1.09, 1.21) <sup>†</sup>	1.15 (1.09, 1.21) <sup>†</sup>
HADS depression (0-21); mean (SD)	4.4 (3.26)	7.3 (4.23)	1.23 (1.15, 1.30) <sup>†</sup>	1.21 (1.14, 1.29) <sup>†</sup>
Catastrophising beliefs (0-6): median (IQR)	0 (0, 2)	3 (0, 5)	1.37 (1.25, 1.51) <sup>†</sup>	1.36 (1.23, 1.50) <sup>†</sup>

OR, Odds Ratio; SD, Standard Deviation; BMI, Body Mass Index; MFPDI, Manchester Foot Pain and Disability Index (higher scores indicate more pain and disability); MTPJ, Metatarsophalangeal Joint; SF12, Short-Form 12 (higher scores indicate better physical and mental health and physical function); PCS, Physical Component Score; MCS, Mental Component Score; HADS, Hospital Anxiety and Depression Scale (higher scores indicate more anxiety and depression); Catastrophising beliefs (higher scores indicate more frequent occurrence); IQR, Inter Quartile Range. <sup>†</sup> per unit increase.



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ACR\_24823\_Figure 2 v2.0400.tif