**Title: Identification of Patterns of Foot and Ankle Pain in the Community: Cross-sectional Findings from the Clinical Assessment Study of the Foot**

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ER provided oversight for the study. CSC and AL led the writing of the paper. MJT, MM, HBM and ER made substantial contributions to study conception, design and data collection. CSC, AL and TR analysed and interpreted data. CSC, AL, TR, MJT, HBM, MM and ER contributed to reviewing the draft paper and approving the final version to be submitted for publication.

**Acknowledgments:**

We would like to thank the administrative, health informatics and research nurse teams of Keele University’s Primary Care Centre Versus Arthritis and the staff of the participating general practices. We would also like to thank Adam Garrow and the © University of Manchester for permission to use the foot manikin (© The University of Manchester 2000. All rights reserved).

**Sources of funding:**

This work was funded by an Arthritis Research UK Programme Grant (18174) and service support through the West Midlands North CLRN. The study funders had no role in the study design; data collection, analysis, or interpretation; in the writing of the paper; or in the decision to submit the paper for publication. MJT was supported by an Integrated Clinical Academic Programme Clinical Lectureship from the National Institute for Health Research (NIHR) and Health Education England (HEE) (ICA-CL-2016-02-014) and is currently supported by an NIHR Development and Skills Enhancement Award (NIHR300818). HBM is currently a National Health and Medical Research Council of Australia Senior Research Fellow (ID: 1135995). The views expressed in this publication are those of the authors and not necessarily those of the NHS, the NIHR, HEE or the Department of Health and Social Care.

**Conflict of interests:** The authors have no financial or other competing interests to declare.

**Abstract**

**Objectives:** To investigate patterns of foot and ankle pain locations and symptoms, socio-demographic and comorbid characteristics to examine whether there are distinct foot and ankle pain phenotypes.

**Methods:** Adults aged ≥50 years registered with four general practices in North Staffordshire were mailed a Health Survey questionnaire. Participants reporting foot pain in the last month indicated foot pain location on a foot manikin. Foot and ankle pain patterns were investigated by latent class analysis. Associations between the classes with foot pain symptoms, socio-demographic and comorbid characteristics were assessed.

**Results:** 4455 participants with complete foot pain and manikin data were included in this analysis (mean age 65 years (SD 9.8), 49% male). Of those with foot and ankle pain (n=1356), 90% had pain in more than one region. Six distinct classes of foot and ankle pain were identified: no pain (71%); bilateral forefoot/midfoot pain (4%), bilateral hindfoot pain (5%), left forefoot/midfoot pain (8%), right forefoot/midfoot pain (5%) and bilateral widespread foot and ankle pain (6%). People with bilateral widespread foot and ankle pain were more likely to be female, obese, depressed, anxious, have/had a manual occupation, have comorbidities, lower SF-12 scores and greater foot-specific disability. Age did not differ between classes.

**Conclusions:** Six distinct classes of foot and ankle pain locations were identified, and those with bilateral widespread foot and ankle pain had distinct characteristics. Further investigation of these individuals is required to determine if they have poorer outcomes over time and whether they would benefit from earlier identification and treatment.

**Word count:** 3088 words

**Key words:** “foot”; “ankle”; “pain”; “phenotypes”; “epidemiology”

**Introduction**

Foot and ankle pain are common in the general population, with frequent foot and ankle pain affecting 13 to 36% and 12 to 15% of adults aged 50 years and over, respectively (Gates et al., 2019; Murray et al., 2018). Foot and ankle pain have significant impact on people’s lives (Menz, Dafour, Katz & Hannan, 2016), with three-quarters of adults aged over 50 years with foot pain experiencing foot pain-related disability on most or all days (Roddy, Muller & Thomas, 2009). There are varied presentations, causes, prognosis, and management options for foot and ankle pain, all of which place a substantial burden on primary care services (Ferguson et al., 2019).

Whilst prevalence of foot and ankle pain as well as its associated risk factors and outcomes have been widely studied (Menz, 2016; Thomas et al., 2011), less is known about patterns of overlap of pain at different sites in the foot and ankle as well as their associated risk factors and outcomes. Many epidemiological studies have reported the occurrence of foot pain as a single entity without considering the location within the foot and ankle complex. Studies which have investigated the location of foot pain reported that toes and forefoot were the most frequently affected, whereas the heel and hindfoot were less commonly involved (Thomas et al., 2011; Gill et al., 2017). Foot and ankle pain are associated with older age, female sex (Parsons, Breen & Foster, 2007), obesity (Dafour et al., 2017), footwear (Dafour et al., 2009), hallux valgus (Menz, Roddy, Thomas & Croft, 2011), osteoarthritis (Kalichman & Hernández-Molina, 2014), and other comorbidities such as rheumatoid arthritis and diabetes (Jaakkola & Mann, 2004; Menz, Barr & Brown, 2011). Foot pain is also associated with adverse outcomes such as poor physical functioning, reduced mobility and falls (Menz & Lord, 2001), and poorer mental health (Awale et al., 2016). However, it is not known whether these risk factors and outcomes are associated with specific foot pain phenotypes.

Although some associations have been established between different types of foot and ankle pain and specific risk factors, foot and ankle pain remains a multifactorial problem with complex physical and psychosocial outcomes, causing substantial associated disability (Keysor et al., 2005). Identifying patterns of symptomatic presentation associated with various risk factors and outcomes may help guide comprehensive assessment and management of foot and ankle pain, as well as to identify those at risk of further progression and increasing disability (Rao, Riskowski & Hannan, 2012).

To date, there have been few studies that have investigated whether foot pain occurs in distinct regions and whether these regions have distinctive characteristics, suggesting different foot pain phenotypes. A recent population-based study of individuals aged 18 years and over identified five foot pain phenotypic presentations using hierarchical cluster analysis where one had predominantly arch and ball pain, one rearfoot pain, one heel pain and two had predominantly forefoot, toe and nail pain; all had distinct age, sex and comorbidity profiles (Gill et al., 2017).

The objective of this study was to investigate patterns of foot and ankle pain locations using latent class analysis (LCA) to determine whether classes of foot and ankle pain exist. We then compared foot pain symptoms, socio-demographic and comorbid characteristics between the different foot and ankle pain classes.

**Materials and Methods**

***Study design***

The Clinical Assessment Study of the Foot (CASF) was a prospective observational cohort study of adults aged ≥50 years registered with four general practices in North Staffordshire, United Kingdom (Roddy et al., 2011). In 2010/2011, a baseline Health Survey questionnaire was mailed to 9334 adults aged 50 years and over, irrespective of any foot-related health care consultation. All participants provided written informed consent. Ethical approval for the study was obtained from the Coventry Research Ethics Committee (REC reference number: 10/H1210/5).

***Foot pain location***

In the baseline Health Survey questionnaire, participants were invited to shade the location of foot pain experienced in the past month on a blank unadorned foot manikin. Foot pain locations were then determined using an overlay foot manikin template (© The University of Manchester 2000. All rights reserved) (Garrow, Silman & Macfarlane, 2004), which has previously been found to be reliable (Chatterton et al., 2013). In the current analysis, seven regions were examined for each foot: great toe, lesser toes, midfoot, plantar heel, posterior non-Achilles, Achilles and ankle.

***Foot pain symptoms, socio-demographic and comorbid characteristics***

The following information was collected in the Health Survey questionnaire: socio-demographics (age, gender, body mass index (BMI) calculated from self-reported height and weight, socioeconomic status, higher education, smoking (never smoked, previously smoked or currently smoking), and ethnicity); foot pain characteristics (duration of foot pain, foot pain in the last year, foot pain, aching or stiffness in the past month, foot pain severity using a 0-10 Numerical Rating Scale (NRS); and body pain regions as indicated on a body manikin. Shading of the body manikin indicating pain was divided into 10 areas: head, neck, shoulder, elbow, hand, chest, abdomen, low back, hip, and knee. Foot and ankle pain-related disability outcomes were also collected: the Manchester Foot Pain and Disability Index (MFPDI) pain and function sub-scales Rasch-transformed scores (Muller & Roddy, 2009), the Short Form-12 (SF-12) physical and mental component scores (Ware, Kosinki & Keller, 1996) and the Hospital Anxiety and Depression Scale (HADS) (Beekman & Verhagen, 2018). Data on previous foot injury and past footwear were also collected. Past footwear use was assessed by line drawings depicting four heel heights (A = flat, B = low, C = medium, and D = high) and four toe-box shapes (A = very wide, B = wide, C = narrow, and D = very narrow). For each period of their life (divided into decades, commencing with 20–29 years of age), participants were asked to indicate which heel height and toe-box shape they wore most of the time (Menz et al., 2016). Self-reported comorbidities were also collected (raised blood pressure, diabetes and circulation problems in the legs). Participants additionally completed the Edinburgh Claudication Questionnaire (Lend & Fowkes, 1992) and self-reported hallux valgus using a validated line-drawing instrument consisting of five drawings for each foot, with each one demonstrating a sequential increase in hallux valgus angle of 15 degrees (Roddy, Zhang & Doherty, 2007). Participants selected the drawing that best depicted the severity of hallux valgus for each foot. Hallux valgus was classed as present in a foot if any of three most severe drawings were selected (Roddy, Zhang & Doherty, 2007). Further details on the data collection methods of descriptive characteristics can be found in the published CASF study protocol (Roddy et al., 2011).

***Statistical analysis***

LCA was used to identify latent classes of participants with similar patterns of foot and ankle pain involvement which are distinct from participants in other classes (Magidson, 1989). LCA was performed on the 14 binary pain regions (seven in each foot). The optimal number of classes was determined by a combination of the following: (1) goodness-of-fit statistics (Akaike Information Criteria [AIC], Bayesian Information Criteria [BIC], sample size-adjusted BIC and the Lo-Mendell-Rubin adjusted likelihood ratio test [LRT] (Nylund, Asparouhov & Muthén, 2007); (2) uncertainty of classification measures (entropy (Shevlin, Dorahy, Adamson & Murphy, 2007) and average posterior probabilities for most likely class membership (Clark, Jones, Wood & Cornelius, 2006)); (3) class size of at least 1% of the sample (Jung & Wickrama, 2008); and (4) clinical relevance and interpretability based on the probabilities for each pain region within each class.

Comparison of participants’ foot and ankle pain symptoms and characteristics between the identified latent classes were made via regression models. Analyses were adjusted for age and gender, which were considered to be potential confounding variables. For continuous data, linear regression was used to estimate marginal means and 95% confidence intervals for each latent class. Significant differences in continuous data between the classes were determined using F-tests. For dichotomous and ordinal data, logistic and ordinal logistic regression was used to estimate average predicted probabilities and 95% confidence intervals respectively for each latent class. Significant differences between the classes were established using chi-square tests.

All analyses were two-tailed and were deemed statistically significant if p<0.05. Analyses was performed using STATA v15 (Stata Corporation, Texas, USA) and LCA was performed using MPLUS v8.3 (Muthén & Muthén, 2013).

**Results**

5109 completed health survey questionnaires were received (adjusted response 56%) (Roddy et al., 2015). Of these, 4455 with complete foot pain and manikin data were included in this analysis. Participants had a mean ± SD age of 65.0 ± 9.8 years and 49% were male (**Table 1**). 1356 (30.4%) reported having foot and ankle pain in the last month in one or more region of either foot and 1215 (27.3%) had pain in two or more foot or ankle regions. The most frequently affected pain regions were the great toe, lesser toes, and the midfoot, with the least commonly affected being the plantar heel and ankle (**Table 2**).

On LCA, the 6-class solution of foot and ankle pain was considered the best fit as the reduction in the AIC and BIC for additional classes was attenuated (**Table 3**). The 6-class solution also had average posterior probabilities for each class that was >0.8 and entropy was high, indicating classes were distinct. All classes comprised at least 1% of the total sample. Although the Lo-Mendell-Rubin LRT showed that 6-class solution did not improve model fit as compared to using the 5-class solution, the 6-class solution further identified participants with left forefoot and midfoot pain, hence differentiating individuals with unilateral forefoot/midfoot symptoms, which was considered to be clinically relevant.

In the 6-class solution, Class 1 was the largest (n=3161, 71.0%) and was characterised by low probabilities of pain in all regions (**Table 4**). Therefore, Class 1 was labelled ‘no pain’. Individuals in class 2 (n=190, 4.3%) had medium to high probabilities of bilateral forefoot/midfoot pain whereas those in class 3 (n=238, 5.3%) had medium to high probabilities of bilateral hindfoot pain, and were therefore labelled accordingly. Participants in classes 4 (n=370, 8.3%) and 5 (n=238, 5.3%) demonstrated similar medium probabilities of having left forefoot and midfoot pain and right forefoot and midfoot pain, respectively and were therefore labelled as left forefoot/midfoot pain and right forefoot/midfoot pain. Class 6 (n=258, 5.8%) had medium to high probabilities across all pain sites and represented bilateral widespread foot and ankle pain. Furthermore, this class contained the highest probabilities for all regions of the foot except the left and right great toe and lesser toes regions compared with other classes.

Following adjustment for age and gender in the regression models, individuals with bilateral widespread foot and ankle pain were more likely to have had pain on ‘all days’ in the past month, had foot pain more than three months in the past year, and experienced greater foot pain severity than the other classes (**Table 5**). Individuals with bilateral widespread foot and ankle pain had higher anxiety and depression scores (HADS), poorer perceived physical and mental health (SF12), and more foot-specific disability (MFPDI) than the other classes.

Individuals in class 2 (bilateral forefoot/midfoot pain) and class 6 (bilateral widespread foot and ankle pain) had a significantly higher probability of being female in comparison to the other classes. Although age and educational status did not differ between foot pain classes, bilateral widespread foot and ankle pain was associated with a higher BMI, a manual occupation, previous bilateral foot injury, and having comorbidities (including diabetes, hypertension, and circulation problems in the legs) than other classes. Individuals in the bilateral forefoot/midfoot pain, bilateral hindfoot pain and bilateral widespread foot and ankle pain classes had higher probabilities of being current or ex-smokers than other classes (**Table 5**).

Previous injury in the right foot was significantly associated with the right forefoot/midfoot pain group and left injury with left forefoot/midfoot pain group (**Table 5**). Higher probabilities of left and right hallux valgus were seen for all classes in comparison to the ‘no pain’ group; the exception to this was left hallux valgus in the right forefoot/midfoot pain group. However, there was no statistically significant differences between patterns of foot and ankle pain and footwear toe-box shape or heel height worn by women between ages 20 and 49 years. Interestingly, a significantly higher proportion of individuals in the bilateral widespread foot and ankle pain group self-reported circulation problems in the legs.

**Discussion**

In this population-based study, approximately one-third of community-dwelling adults aged 50 years and over reported foot and ankle pain. Using LCA, we found six distinct phenotypes based on foot pain locations: no pain, bilateral forefoot/midfoot pain, bilateral hindfoot pain, left forefoot/midfoot pain, right forefoot/midfoot pain, and bilateral widespread foot and ankle pain. The bilateral widespread foot and ankle pain class had more frequent and severe foot pain, longer foot pain duration, poorer perceived general health, worse anxiety and depression, and greater foot-specific functional limitation than other classes. Individuals in this class were also more likely to be female, obese, and have comorbidities including hallux valgus, diabetes, hypertension, and circulation problems in the legs. The unilateral forefoot/midfoot pain classes were associated with history of ipsilateral foot injury.

There are few existing studies that have taken similar approaches to explore patterns of foot and ankle pain locations. The North West Adelaide Health Study, which was a community-based study undertaken in Adelaide, Australia identified five foot pain clusters using hierarchical cluster analysis: one with predominantly ball and arch pain (27%); one with rearfoot pain (21%); another with heel pain (13%), and two with predominantly forefoot, toe and nail pain (28% and 11%) (Gill et al., 2017). The aforementioned study had a similarly large sample size compared to our study, although there were higher proportions of individuals in our study who reported foot and ankle pain (30% versus 17%) (Gill et al., 2017). We similarly identified individuals who were classed as predominantly forefoot and hindfoot groups, and found that forefoot pain was the most common presentation. The North West Adelaide Health Study, however, did not identify a bilateral widespread foot and ankle pain group, and found clusters characterised by predominantly ball and arch pain as well as heel pain. These differences could be explained by their population being younger than ours (≥18 years compared to ≥50 years), and their use of the Framingham foot manikin (Hannan et al., 2006) which required participants to have pain on “most days”, whilst our study used the Garrow foot manikin (Garrow, Silman & Macfarlane, 2004) in which study participants were asked to shade the foot regions where they experienced pain in the past month. In the current study, the foot manikin was divided into 14 foot and ankle pain regions (seven regions on each foot), whereas the Adelaide study (Gill et al., 2017) divided foot pain into seven areas that were recorded across both feet. Therefore, our analysis provides the added advantage of being able to compare patient characteristics of unilateral foot pain symptoms to those with bilateral foot and ankle pain, in addition to evaluating patient characteristics of different foot pain regions (forefoot, midfoot and/or hindfoot). Furthermore, our study used LCA, a robust model-based clustering approach that has been used in a number of musculoskeletal population-based studies to help characterise challenging and varied symptomatic presentations, as well as to identify distinctive classes of foot and ankle pain (de Luca et al., 2017; Rathod et al., 2016). The advantage of using LCA is that the choice of the number of classes is less arbitrary compared to hierarchical cluster analysis (Schreiber & Pekarik, 2014).

We found a significant association between female sex and bilateral widespread foot and ankle pain class, but no association was seen between age and any of the classes. This is contrary to the results found by the North West Adelaide Health Study (Gill et al., 2017) which found forefoot, toe and nail pain occurring in older men, rearfoot and heel pain affected a high proportion of young individuals, and ball and arch pain was seen in younger females. The differences may be explained by the older population in our study where more individuals might have osteoarthritis and other chronic conditions than the North West Adelaide Health Study (Gill et al., 2017), where study participants ranged between 20 to over 75 years of age and were more likely to be affected by a broader range of foot conditions. Our findings showed that bilateral widespread foot and ankle pain is associated with significant problems beyond localised pain, including impaired physical and mental health, and comorbidities such as obesity, diabetes, hypertension and circulation problems of the legs after adjusting for age and gender, confirming the results of a previous separate analyses from the North West Adelaide Health Study (Hill, Gill, Menz & Taylor, 2008). Our study also showed higher proportions of those with bilateral widespread foot and ankle pain who had worked in manual occupations, and had higher depression and anxiety scores. Many previous studies have shown that foot problems are more common in older people with multiple chronic disease including diabetes and arthritis (Barr et al., 2005; Otter et al., 2010). There is also a relationship between obesity and depression (Amiri, Behnezhad & Nadinlui, 2018), indicating the likelihood of a complex interplay of the aforementioned factors and comorbidities, and supporting the association between these factors and foot pain. Consistent with previous studies (Hill, Gill, Menz & Taylor, 2008; Keenen et al., 2006), we found strong associations between reported foot pain and pain in other regions of the body, suggesting that foot pain symptoms of our study population may be part of a generalised form of osteoarthritis or systemic pain condition (Nelson, Smith, Golightly & Jordan, 2014).

Higher prevalence of foot pain in women has been attributed to the wearing of shoes with high heels and narrow toe box, as well as to the development of hallux valgus (Menz et al., 2016). However, our study did not show any statistically significant differences between foot and ankle pain patterns and either footwear toe-box shape or heel height. Higher probabilities of individuals classified as having hallux valgus were present in the classes that had forefoot pain (bilateral forefoot/midfoot pain, left forefoot/midfoot pain and right forefoot/midfoot pain).

*Strengths and limitations*

Strengths of our study include a large sample size, the population-based setting and the inclusion of ankle pain as well as foot pain. Limitations of our study are worthy of acknowledgement. The response to the postal health survey questionnaire was lower than we had expected despite the use of several strategies to maximise response. However, responders did not differ significantly from the mailed population by age, gender or practice distribution (Roddy et al., 2015). Furthermore, our study included only individuals aged 50 years and above and had a low representation of ethnic minority groups. In addition, the cross-sectional observational study design cannot elucidate temporal aspects of associations or causality.

In conclusion, this detailed analysis of pattern of foot and ankle pain phenotypes in a primary care cohort identified six distinct classes based on foot pain location. Individuals with bilateral widespread foot and ankle pain were distinct from other subgroups in terms of foot and ankle pain symptoms, foot-related disability, were more obese and had more comorbidities including poorer mental health, diabetes and hypertension. Hallux valgus and foot injury were associated with specific forefoot/midfoot pain phenotypes. Our findings provided new insights and a greater understanding of the patterns of foot and ankle pain in the community. Knowledge and awareness of these foot and ankle pain patterns highlights opportunities to examine their outcome over time, and to provide more targeted preventive strategies and treatments for at-risk individuals. Further investigation of individuals especially with bilateral widespread foot and ankle pain is also needed to determine if they have poorer outcomes over time and whether they would benefit from earlier identification and treatment.

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**Table 1** Socio-demographic characteristics of the study participants

|  |  |
| --- | --- |
| **Characteristics** | **% (Number)** |
| Female gender | 50.8 (2261) |
| Age group, years, mean (SD) | 1. (9.8) |
| BMI, kg/m2, mean (SD)   * Missing | 27.4 (5.1)  4.3 (191) |
| Higher education   * Yes * No * Missing | 17.1 (762)  78.8 (3510)  4.1 (183) |
| Socioeconomic status   * Managerial/administrative/professional * Intermediate/self or small employers * Routine/Manual/Technical * Missing | 20.9 (929)  18.1 (804)  52.0 (2315)  9.1 (407) |
| Smoking   * Never smoked * Previously smoked * Currently smoking * Missing | 45.2 (2012)  38.7 (1723)  15.2 (675)  1.0 (45) |
| Ethnicity   * White UK/ European * Afro Caribbean * Chinese * Asian * African * Other * Missing | 95.5 (4255)  0.3 (12)  0.2 (11)  0.7 (33)  0.2 (7)  0.5 (23)  2.6 (114) |

*Values are in number and percentages unless stated otherwise*

**Table 2** Location of foot pain among 4455 study participants aged ≥50 years

|  |  |  |  |
| --- | --- | --- | --- |
| **Total number of areas of foot pain** | **Left foot, % (Number)** | **Right foot, % (Number)** | **Left and right foot combined, % (Number)** |
| 0 | 75.6 (3364) | 75.5 (3365) | 69.6 (3099) |
| 1 | 4.0 (180) | 4.7 (209) | 3.2 (141) |
| 2 | 6.4 (286) | 6.2 (276) | 5.4 (240) |
| 3 | 4.8 (212) | 4.8 (213) | 4.0 (178) |
| 4 | 3.7 (163) | 3.4 (152) | 4.7 (208) |
| 5 | 2.3 (103) | 2.3 (101) | 2.1 (94) |
| 6 | 2.0 (90) | 1.7 (76) | 2.6 (115) |
| 7 | 1.3 (57) | 1.4 (63) | 1.2 (52) |
| 8 | - | - | 2.2 (96) |
| 9 | - | - | 0.9 (40) |
| 10 | - | - | 1.3 (59) |
| 11 | - | - | 0.5 (24) |
| 12 | - | - | 1.1 (50) |
| 13 | - | - | 0.3 (15) |
| 14 | - | - | 1.0 (44) |
| **Different areas of foot pain** | **Left foot, % (Number)** | **Right foot, % (Number)** | **Both feet, % (Number)** |
| Great toe | 15.4 (686) | 15.3 (681) | 11.2 (497) |
| Lesser toes | 13.5 (602) | 13.9 (619) | 9.6 (426) |
| Midfoot | 13.7 (612) | 13.3 (592) | 8.7 (388) |
| Plantar heel | 6.0 (267) | 5.6 (249) | 4.1 (183) |
| Posterior non-Achilles | 11.6 (515) | 10.9 (487) | 7.9 (354) |
| Achilles | 9.2 (409) | 9.1 (406) | 6.7 (298) |
| Ankle | 9.1 (403) | 8.4 (376) | 6.2 (274) |

**Table 3.** Model fit statistics from latent class analysis

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **No. of classes** | **AIC** | **BIC** | **Sample-size adjusted BIC** | **Entropy** | **Lo-Mendell-Rubin adjusted LRT p-value** | **Smallest average posterior probabilities** | **Smallest class size %** |
| 1 | 42783.0 | 42872.7 | 42828.2 | - | - | 1.000 | 100 |
| 2 | 28994.9 | 29180.6 | 29088.4 | 0.955 | <0.001 | 0.969 | 26.0 |
| 3 | 26990.9 | 27272.6 | 27132.8 | 0.944 | 0.0005 | 0.919 | 6.8 |
| 4 | 25911.2 | 26288.9 | 26101.4 | 0.943 | <0.001 | 0.914 | 6.3 |
| 5 | 25452.6 | 25926.3 | 25691.2 | 0.948 | <0.001 | 0.848 | 5.3 |
| **6** | **25109.0** | **25678.7** | **25395.9** | **0.939** | **0.3826** | **0.863** | **4.3** |
| 7 | 24809.4 | 25475.1 | 25144.7 | 0.943 | 0.0836 | 0.867 | 3.1 |
| 8 | 24578.9 | 25340.7 | 24962.6 | 0.950 | 0.1891 | 0.883 | 2.0 |
| 9 | 24346.7 | 25204.5 | 24778.7 | 0.955 | 0.0623 | 0.864 | 1.6 |

*AIC, Akaike Information Criteria; BIC, Bayesian Information Criteria; LRT, likelihood ratio test. The bold text indicates the model that was selected as having the optimal number of classes.*

**Table 4** Probabilities of foot and ankle pain regions in each latent class

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Classes | **Class 1: No Pain** | **Class 2: Bilateral forefoot/midfoot pain** | **Class 3: Bilateral hindfoot pain** | **Class 4: Left forefoot/midfoot pain** | **Class 5: Right forefoot/midfoot pain** | **Class 6: Bilateral widespread foot and ankle pain** |
| Class size % (Number) based on most likely latent class membership | 71.0 (3161) | 4.3 (190) | 5.3 (238) | 8.3 (370) | 5.3 (238) | 5.8 (258) |
| Average posterior probabilities for most likely latest class membership | 0.987 | 0.942 | 0.909 | 0.863 | 0.898 | 0.949 |
| Left great toe | 0.004 | 0.952 | 0.132 | 0.546 | 0.060 | 0.940 |
| Left lesser toes | 0.001 | 0.971 | 0.118 | 0.406 | 0.007 | 0.900 |
| Left midfoot | <0.001 | 0.565 | 0.438 | 0.514 | <0.001 | 0.798 |
| Left plantar heel | <0.001 | 0.176 | 0.223 | 0.149 | 0.001 | 0.480 |
| Left posterior non-Achilles | 0.001 | 0.145 | 0.804 | 0.113 | 0.063 | 0.884 |
| Left Achilles heel | <0.001 | 0.033 | 0.680 | 0.035 | 0.039 | 0.825 |
| Left ankle pain | 0.001 | 0.197 | 0.508 | 0.213 | <0.001 | 0.617 |
| Right great toe | 0.007 | 0.948 | 0.082 | 0.245 | 0.508 | 0.933 |
| Right lesser toes | 0.003 | 0.983 | 0.079 | 0.099 | 0.533 | 0.907 |
| Right midfoot | 0.001 | 0.592 | 0.265 | 0.177 | 0.592 | 0.775 |
| Right plantar heel pain | <0.001 | 0.168 | 0.132 | 0.048 | 0.170 | 0.487 |
| Right posterior non-Achilles | <0.001 | 0.126 | 0.552 | 0.049 | 0.339 | 0.874 |
| Right Achilles heel | 0.001 | 0.019 | 0.473 | 0.020 | 0.282 | 0.801 |
| Right ankle pain | <0.001 | 0.160 | 0.357 | 0.084 | 0.275 | 0.617 |

*Values are probabilities unless indicated otherwise*.

**Table 5** Foot and ankle pain symptoms and their related disabilities, demographic and comorbid characteristics of the six distinct classes of foot and ankle pain\*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Class 1: No Pain**† | **Class 2: Bilateral forefoot/midfoot pain**† | **Class 3: Bilateral hindfoot pain**† | **Class 4: Left forefoot/midfoot pain**† | **Class 5: Right forefoot/midfoot pain**† | **Class 6: Bilateral widespread foot and ankle pain**† | **Difference between the 6 classes (Significance)** † |
| Frequency, % (Number) | 71.0 (3161) | 4.3 (190) | 5.3 (238) | 8.3 (370) | 5.3 (238) | 5.8 (258) | - |
| **Foot and ankle pain symptoms and related disability** | | | | | | | |
| Pain >1 day in any part of body in the past month | 1389; 0.49 (0.47, 0.50) | 157; 0.90 (0.85, 0.94) | 199; 0.90 (0.86, 0.94) | 296; 0.85 (0.81, 0.89) | 188; 0.83 (0.78, 0.88) | 233; 0.96 (0.94, 0.99) | ꭕ2=432.47  P<0.001 |
| Duration of foot pain in the past month |  | | | | | | |
| * No days | 609; 0.63 (0.60, 0.66) | 2; 0.03 (0.02, 0.04) | 4; 0.04 (0.03, 0.06) | 7; 0.07 (0.05,0.08) | 7; 0.07 (0.05, 0.08) | 1; 0.02 (0.01, 0.02) | ꭕ2=1131.22  P<0.001 |
| * Few days | 142; 0.20 (0.18, 0.22) | 18; 0.06 (0.04, 0.07) | 27; 0.07 (0.05, 0.09) | 49; 0.10 (0.08, 0.12) | 34; 0.10 (0.08, 0.12) | 6; 0.03 (0.02, 0.04) |
| * Some days | 139; 0.13 (0.11, 0.15) | 42; 0.22 (0.19, 0.26) | 56; 0.26 (0.22, 0.30) | 125; 0.32 (0.29, 0.35) | 74; 0.32 (0.28, 0.35) | 29; 0.13 (0.10, 0.16) |
| * Most days | 41; 0.03 (0.03, 0.04) | 62; 0.37 (0.34, 0.40) | 83; 0.36 (0.34, 0.39) | 119; 0.33 (0.30, 0.36) | 70; 0.33 (0.30, 0.36) | 97; 0.32 (0.29, 0.36) |
| * All days | 13; 0.01 (0.01, 0.01) | 64; 0.32 (0.26, 0.38) | 62; 0.26 (0.21, 0.31) | 64; 0.18 (0.15, 0.22) | 44; 0.18 (0.14, 0.22) | 123; 0.50 (0.44, 0.56) |
| Duration of foot pain last 12 months |  | | | | | | |
| * <7 days | 188; 0.40 (0.36, 0.44) | 18; 0.07 (0.05, 0.09) | 29; 0.10 (0.08, 0.13) | 39; 0.13 (0.11, 0.16) | 30; 0.14 (0.11, 0.17) | 10; 0.05 (0.04, 0.07) | ꭕ2=311.19  P<0.001 |
| * 1-4 weeks | 87; 0.22 (0.19, 0.24) | 16; 0.09 (0.06, 0.11) | 26; 0.11 (0.09, 0.14) | 65; 0.14 (0.11, 0.16) | 35; 0.14 (0.11, 0.17) | 14; 0.06 (0.05, 0.08) |
| * >1 month but <3 months | 70; 0.14 (0.12, 0.16) | 13; 0.10 (0.08, 0.13) | 24; 0.13 (0.11, 0.15) | 48; 0.14 (0.12, 0.16) | 39; 0.15 (0.13, 0.17) | 28; 0.08 (0.06, 0.10) |
| * ≥3 months | 112; 0.25 (0.21, 0.28) | 143; 0.74 (0.68, 0.80) | 156; 0.65 (0.59, 0.71) | 218; 0.59 (0.54, 0.64) | 133; 0.57 (0.51, 0.63) | 206; 0.80 (0.76, 0.85) |
| Foot pain severity (0-10), (Mean 95% CI) | 1.65 (1.50, 1.82) | 5.92 (5.59, 6.24) | 6.04 (5.75, 6.33) | 5.35 (5.12, 5.59) | 5.42 (5.13, 5.71) | 7.20 (6.92, 7.48) | F= 356.38 P<0.001 |
| PCS SF-12, mean (95% CI) § | 44.73 (44.33, 45.13) | 35.91 (34.26, 37.55) | 33.50 (32.00, 34.99) | 39.06 (37.89, 40.22) | 38.30 (36.82, 39.78) | 29.12 (27.68, 30.55) | F= 141.98 P<0.001 |
| MCS SF-12, mean (95% CI) § | 51.06 (50.66, 51.46) | 45.85 (44.20, 47.50) | 45.11 (43.61, 46.60) | 47.76 (46.59, 48.93) | 48.42 (46.93, 49.90) | 41.40 (39.96, 42.84) | F=48.19  P<0.001 |
| HADS depression score, mean (95% CI) ¶ | 4.35 (4.21, 4.49) | 6.52 (5.97, 7.08) | 7.35 (6.86, 7.85) | 5.85 (5.46, 6.25) | 6.11 (5.61, 6.61) | 8.87 (8.39, 9.34) | F= 97.51 P<0.001 |
| HADS anxiety score, mean (95% CI) ¶ | 5.81 (5.67, 5.96) | 8.02 (7.42, 8.63) | 8.46 (7.92, 9.01) | 7.80 (7.36, 8.23) | 7.31 (6.76, 7.85) | 10.15 (9.63, 10.67) | F= 76.43 P<0.001 |
| MFPDI pain subscale, mean (95% CI) ‡ | -1.75 (-1.88, -1.62) | 0.32 (0.13, 0.51) | 0.03 (-0.14, 0.20) | -0.31 (-0.45, -0.18) | -0.28 (-0.45, -0.11) | 0.99 (0.83, 1.15) | F=156.23 P<0.001 |
| MFPDI function subscale, mean (95% CI) ‡ | -1.99 (-2.17, -1.81) | -0.02 (-0.28, 0.24) | 0.30 (0.06, 0.53) | -0.68 (-0.87, -0.49) | -0.56 (-0.80, -0.33) | 1.39 (1.17, 1.62) | F=120.73 P<0.001 |
| **Socio-demographic and comorbid characteristics** | | | | | | | |
| Age, mean (95% CI) years †† | 65.07 (64.72, 65.41) | 66.46 (65.06, 67.86) | 64.57 (63.32, 65.81) | 64.88 (63.88, 65.88) | 63.97 (62.72, 65.21) | 64.64 (63.44, 65.84) | F=1.57  P= 0.165 |
| Female sex \*\* | 1519; 0.48 (0.46, 0.50) | 119; 0.62 (0.56, 0.69) | 135; 0.56 (0.50, 0.62) | 208; 0.56 (0.51, 0.61) | 123; 0.52 (0.46, 0.58) | 157; 0.61 (0.55, 0.66) | ꭕ2=36.47  P<0.001 |
| BMI, mean (95%CI) kg/m2 | 26.80 (26.63, 26.98) | 28.29 (27.57, 29.00) | 29.46 (28.82, 30.11) | 27.52 (27.01, 28.04) | 28.68 (28.04, 29.32) | 31.04 (30.42, 31.65) | F=47.37 P<0.001 |
| Ever smoker versus never smoker | 1652; 0.52 (0.51, 0.54) | 109; 0.60 (0.53, 0.67) | 147; 0.63 (0.57, 0.69) | 206; 0.57 (0.52, 0.62) | 134; 0.57 (0.50, 0.63) | 150; 0.60 (0.54, 0.66) | ꭕ2=20.93  P<0.001 |
| Attended higher education | 533; 0.18 (0.16, 0.19) | 32; 0.18 (0.12, 0.24) | 38; 0.16 (0.12, 0.21) | 72; 0.20 (0.16, 0.24) | 46; 0.20 (0.15; 0.25) | 41; 0.16 (0.12, 0.21) | ꭕ2= 2.31  P=0.805 |
| Socioeconomic status (Manual vs. non-manual occupation) | 1579; 0.55 (0.53, 0.57) | 97; 0.58 (0.50, 0.66) | 144; 0.66 (0.60, 0.73) | 202; 0.59 (0.54, 0.64) | 135; 0.61 (0.55, 0.68) | 158;0.70 (0.64, 0.76) | ꭕ2= 29.46 p<0.001 |
| High/very high-heeled footwear ever worn between ages 20 and 49 years # | 967; 0.76 (0.74, 0.78) | 88; 0.79 (0.72, 0.87) | 84; 0.74 (0.66, 0.82) | 144; 0.77 (0.71, 0.83) | 83; 0.75 (0.67, 0.83) | 103; 0.77 (0.69, 0.84) | ꭕ2=1.05  P=0.959 |
| Narrow/very narrow toe box ever worn between ages 20 and 49 years ## | 1052; 0.83 (0.81, 0.85) | 100; 0.91 (0.86, 0.96) | 99; 0.88 (0.82, 0.94) | 166; 0.89 (0.84, 0.93) | 89; 0.82 (0.74, 0.89) | 113; 0.85 (0.79, 0.91) | ꭕ2=9.38  P=0.095 |
| Left hallux valgus ‡‡ | 623; 0.21 (0.20, 0.22) | 72; 0.36 (0.29, 0.42) | 74; 0.31 (0.25, 0.37) | 136; 0.37 (0.32, 0.42) | 51; 0.22 (0.17, 0.28) | 105; 0.41 (0.35, 0.47) | ꭕ2=107.76  P<0.001 |
| Right hallux valgus ‡‡ | 640; 0.22 (0.20, 0.23) | 74; 0.37 (0.30, 0.43) | 69; 0.29 (0.23, 0.35) | 130; 0.36 (0.31, 0.41) | 76; 0.33 (0.27, 0.39) | 106; 0.42 (0.36, 0.48) | ꭕ2=98.28  P<0.001 |
| Previous foot injury |  | | | | | | |
| * Right | 96; 0.11 (0.09, 0.13) | 16; 0.09 (0.05, 0.13) | 27; 0.11 (0.07, 0.15) | 31; 0.09 (0.06, 0.11) | 85; 0.36 (0.30, 0.42) | 30; 0.12 (0.08, 0.16) | ꭕ2=89.79  P<0.001 |
| * Left | 71; 0.08 (0.06, 0.10) | 11; 0.06 (0.03, 0.09) | 41; 0.18 (0.13, 0.22) | 75; 0.21 (0.17, 0.25) | 11; 0.05 (0.02, 0.07) | 25; 0.10 (0.06, 0.14) | ꭕ2=59.11  P<0.001 |
| * Bilateral | 28; 0.03 (0.02, 0.04) | 15; 0.08 (0.04, 0.13) | 25; 0.11 (0.07, 0.15) | 28; 0.08 (0.05, 0.10) | 12; 0.05 (0.02, 0.08) | 49; 0.19 (0.15, 0.24) | ꭕ2=70.40  P<0.001 |
| Diabetes mellitus ¥ | 375; 0.12 (0.11, 0.13) | 36; 0.19 (0.13, 0.24) | 36; 0.16 (0.11, 0.20) | 37; 0.10 (0.07, 0.13) | 38; 0.17 (0.12, 0.21) | 66; 0.26 (0.21, 0.32) | ꭕ2=53.36  P<0.001 |
| Hypertension ¥ | 1230; 0.39 (0.37, 0.40) | 86; 0.44 (0.37, 0.51) | 127; 0.54 (0.48, 0.60) | 179; 0.49 (0.44, 0.54) | 110; 0.47 (0.41, 0.53) | 157; 0.62 (0.56, 0.67) | ꭕ2=78.41  P<0.001 |
| Circulation problems in the legs ¥ | 546; 0.17 (0.16, 0.19) | 87; 0.44 (0.37, 0.51) | 103; 0.43 (0.37, 0.50) | 105; 0.28 (0.24, 0.33) | 73; 0.32 (0.26, 0.38) | 152; 0.59 (0.53, 0.65) | ꭕ2=321.33  P<0.001 |
| Intermittent claudication ¥¥ | 206; 0.07 (0.06, 0.08) | 12; 0.08 (0.04, 0.12) | 15; 0.08 (0.04, 0.011) | 36; 0.12 (0.08, 0.16) | 20; 0.10 (0.06, 0.14) | 12; 0.05 (0.02, 0.08) | ꭕ2=10.84  P=0.055 |

*\*Values are the number; Probability (95% confidence interval [95%CI]) unless indicated otherwise.*

BMI= body mass index; PCS= Physical component score; MCS= Mental Component Score; SF-12= Short Form 12 health survey; HADS= Hospital anxiety and depression scale; MFPDI= Manchester Foot Pain and Disability Index.

† Adjusted for age and gender

†† Adjusted for gender only

\*\* Adjusted for age only

§ Lower scores on the SF-12 indicate poorer physical and mental health

¶ Higher scores on the HADS indicate more severe anxiety and depression

‡ Positive scores on the Rasched MFPDI indicate more pain and functional impairment

# Exposure was restricted to females and defined as previous high or very high footwear worn on most days for at least one 10-year period between ages 20 and 49 years

## Defined as previous narrow or very narrow toe box footwear worn on most days for at least one 10-year period between ages 20 and 49 years.

‡‡ Hallux valgus was determined by self-report from line drawings of each foot that depicted increasing grades in the hallux valgus angle of 15 degree.

¥ Self-reported comorbidities

¥¥ Defined using Edinburgh Claudication Questionnaire