Prevalence of foot pain across an international consortium of population based cohorts

Authors: Lucy S Gates PhD[1,2,3], Nigel K Arden MD[3,4,5], Marian T Hannan DSc MPH[6], Edward Roddy DM[7,8], Tiffany K Gill MAppSc PhD[9], Catherine L Hill MBBS MD[9,10], Alyssa B Dufour PhD[6], Trishna Rathod-Mistry MSc[7], Martin J Thomas PhD[7,8], Hylton B Menz PhD DSc[11], Catherine J Bowen PhD[1,2], Yvonne M Golightly PT MS PhD[12, 13, 14, 15]

Institutions:

1. Faculty of Health Sciences, University of Southampton, Southampton, UK
2. Arthritis Research UK Sports, Exercise and Osteoarthritis Centre of Excellence, University of Southampton, Southampton, UK
3. Arthritis Research UK Sports, Exercise and Osteoarthritis Centre of Excellence, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK
4. MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK
5. Medical School, University of Sydney, Australia
6. Institute for Aging Research, Hebrew SeniorLife, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA
7. Arthritis Research UK Primary Care Centre, Research Institute for Primary Care & Health Sciences, Keele University, Staffordshire, ST5 5BG, UK
8. Haywood Academic Rheumatology Centre, Midlands Partnership NHS Trust, Haywood Hospital, Burslem, Staffordshire, ST6 7AG, UK
9. Adelaide Medical School, The University of Adelaide, Adelaide, South Australia, Australia
10. Rheumatology Department, The Queen Elizabeth Hospital, Woodville, South Australia, Australia
11. School of Allied Health, College of Science, Health and Engineering, La Trobe University, Melbourne, Victoria, Australia
12. Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, USA
13. Thurston Arthritis Research Center, University of North Carolina, Chapel Hill, NC, USA
14. Injury Prevention Research Center, University of North Carolina, Chapel Hill, NC, USA

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15. Division of Physical Therapy, University of North Carolina, Chapel Hill, NC, USA

Corresponding author: Lucy Gates
University of Southampton, Health Sciences, 12 University Rd, Southampton, UK, SO17 1BJ
L.gates@soton.ac.uk
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Abstract

Objective. Despite the potential burden of foot pain, some of the most fundamental epidemiological questions surrounding the foot remain poorly explored. The prevalence of foot pain has proved difficult to compare across existing studies due to variations in case definitions. The objective of this study was to investigate the prevalence of foot pain in a number of international population-based cohorts usinge original data and to explore differences in the case definitions used. ~~and create a single harmonised definition to investigate the prevalence of foot pain in a number of international population-based cohorts~~.

Methods. Foot pain variables were examined in five cohorts (the Chingford Women Study, the Johnston County Osteoarthritis Project, the Framingham Foot Study, the Clinical Assessment Study of the Foot and the North West Adelaide Health Study). One foot pain question was chosen from each cohort based on its similarity to the American College of Rheumatology (ACR) pain question.

Results. The precise definition of foot pain varied between the cohorts. The prevalence of foot pain ranged from 13 to 36% and was lowest within the cohort that used a case definition specific to pain, compared to the four remaining cohorts that included components of pain, aching or stiffness. Foot pain was generally more prevalent in women, the obese and generally increased with age, being much lower in younger participants (20-44 years).

Conclusion. Foot pain is common and is associated with female sex, older age and obesity. The prevalence of foot pain is likely affected by the case definition used,

64 therefore consideration must be given for future population studies to use consistent
65 measures of data collection.
66

Significance and Innovations

- ~~Harmonisation~~ Comparison of original ~~of~~ data is a key component to effectively enhancing scientific content and value of large studies, both past and current. This study is the first effort to do so in an under-studied yet common concern in rheumatology – foot pain
- As seen with data harmonisation of knee outcomes, the prevalence of foot pain is likely affected by the case definition used
- Rather than using summary estimates of effect in future work, the use of original participant data across cohorts allows for a more detailed consideration of the heterogeneity in variable case definitions
- Consideration must be given for future population studies to use more consistent measures of data collection

Introduction

Foot pain has been identified as an independent risk factor for locomotor disability [1], impaired balance [2] increased risk of falls [3, 4], loss of independence, and reduced quality of life [5]. It is likely that foot pain contributes a significant burden on both older individuals and healthcare systems. The literature suggests that foot pain is highly prevalent in the general population, however prevalence estimates vary between 9% and 30% [6-9]. Foot problems have been reported to account for up to 8% of a general practitioner's musculoskeletal caseload in the UK [10, 11].

Despite the potential burden of foot pain, to date, some of the most fundamental epidemiological questions surrounding the foot remain poorly explored, particularly with consideration to basic demographic features. Accurately estimating the burden of foot pain among the general population is important so that clinical and cost-effective management strategies can be implemented. Estimating the proportion of a population with a condition such as foot pain will provide the basis for determining the number of people who may require care, for monitoring changes in condition occurrence over time, An investigation of foot pain prevalence using original data in a number of international population-based cohorts would enable differences in foot pain frequency between ~~across~~ geographical regions and sociodemographic groups, with consideration of age, sex, body mass index (BMI) and race to be determined~~.~~ Frequencies obtained from research ~~Prevalence estimates would also provide a foundation to establishing the reasons for differences in such figures~~are the basis for probability estimates for the purposes of patient care and

future research can begin to establish potential risk factors for foot pain and associated conditions.

Traditional meta-analyses can be valuable and efficient in terms of time and resources required, but can suffer from several substantial limitations. They are limited to published results and may therefore suffer from publication bias and the quality and availability of data may vary across studies [12]. Such issues have been previously encountered due to the considerable variation used in case definitions for type, period and patterns of pain, which limited the ability to pool data and provide accurate prevalence estimates [7]. The heterogeneity of variable case definitions is a limitation to any research looking to compare data across cohorts or study data sets. It is necessary to examine identify the components and definitions of each variable and where possible produce a method to standardise of harmonisation for each variable. Such methods have been previously highlighted in the investigation of knee osteoarthritis (OA) [13, 14].

Therefore, the primary aim of this study was to identify the prevalence of foot pain in five prospective cohorts using original participant data. The secondary aim was to consider and investigate potential reasons for differences in pain across geographical locations stratified byaccording to important factors, including such as age, sex, BMI and race, selection bias in each cohort (sampling method, response rate and loss to follow-up) and measurement bias , with consideration of (foot pain case definitions). The cross-sectional study makes use of original data from five international population cohorts linked to a consortium of international foot collaborators, with the aim to harmonise case definitions of each variable to create a single standardised definition of foot pain across five cohorts.

Early findings from a cross-cohort foot osteoarthritis collaboration project with principal investigators from prospective cohorts including the Chingford Women Study, the Johnston County Osteoarthritis Project and the Framingham Foot Study ~~Chingford Women Study~~, revealed a need to establish a larger consortium of foot and ankle collaborators to address the variations in data collection across population cohorts. In 2017 a consortium of international collaborators was formed to encourage a more collaborative approach to foot and ankle research. The consortium consisted of principle investigators and researchers associated with current epidemiological foot and ankle cohort studies and representative research. Potential cohorts for the current study were identified through members of the consortium with knowledge of prospective population based cohorts rich in foot pain data. ~~that were not enhanced for risk factors of lower limb musculoskeletal disease.~~ The Chingford Women Study [15]~~[15][15][15][15][15][15][15]~~, the Johnston County Osteoarthritis Project [16], the Clinical Assessment Study of the Foot [17]~~[17][17][17][16][16][16][16][16]~~, the Framingham Foot Study [18] and the North West Adelaide Health Study were identified [19].

Chingford Women Study

The Chingford Women Study is an ongoing prospective population-based longitudinal cohort of women, established to assess risk factors and associations with osteoporosis and OA [15]. The cohort originally consisted of 1003 women aged 45-64 years recruited from a

general practice in Chingford, North-East London, United Kingdom (UK). Since 1989 the women have been assessed almost annually with a number of investigations. The current study used data from year 15 (2003).

Johnston County Osteoarthritis Project

The Johnston County Osteoarthritis Project is an ongoing, population-based longitudinal study, established to investigate the epidemiology of OA among African Americans and Caucasians residing in six townships in a mostly rural county in North Carolina, United States of America (USA) [16]. Participants recruited to this study were civilian, non-institutionalized residents who were at least 45 years old. The original cohort included participants enrolled between 1991 and 1997. Data for the present analysis were from the first follow-up visit (T1), collected during 1999-2004.

Clinical Assessment Study of the Foot

The Clinical Assessment Study of the Foot is an ongoing population-based prospective observational cohort study of foot pain and foot OA [17]. All adults aged 50 years and over registered with four general practices in North Staffordshire, UK were invited to take part in the study, irrespective of consultation for foot pain or problems. The present study uses data from the initial baseline health survey questionnaire mailed in 2010/2011, which gathered information on aspects of general health, including foot pain.

Framingham Foot Study

The Framingham Foot Study includes members of the Framingham Heart Study Original Cohort, the Framingham Heart Study Offspring Cohort, and a third community sample [18]. The Original Cohort was formed in 1948 from a two-thirds sample of the town of Framingham, Massachusetts~~MA~~, USA in order to study risk factors for heart disease and has been examined biennially [20]. In 1972, the offspring and spouses of the offspring formed the Offspring Cohort to study familial risk factors for heart disease and have been examined every four years [21]. The community sample was derived from census-based, random-digit dialling within the Framingham community contacting subjects who were >50 years old and ambulatory in order to increase participation by minorities. Data for the present analysis were collected between 2002 and 2008.

North West Adelaide Health Study

The North West Adelaide Health Study is a longitudinal study of randomly selected adults aged 18 years and over at the time of recruitment (1999 to 2003) from the North-West region of Adelaide, South Australia. It aims to increase the ability of strategies and policies to prevent, detect and manage a range of chronic conditions [19]. Participant information was obtained from a Computer Assisted Telephone Interview (CATI), a self-completed questionnaire and a clinic assessment at each stage [19, 22]. The present study used data collected in stage 2 (2004-2006).

Inclusion criteria

Across all included cohorts, participants who had responded to the foot pain question were selected for analysis. Where available, age, sex, BMI and race were also extracted for each participant.

Statistical analysis

Descriptive data for demographic characteristics of each cohort were calculated using means and standard deviations or frequencies and percentages, as appropriate. Prevalence and 95% confidence intervals were also calculated for foot pain by age, sex, BMI and race for each cohort. Sensitivity analysis was undertaken on The Chingford Women Study to estimate foot pain prevalence with adjusted cut off points (6+ /15+ days).

The Chingford Women Study and Johnston County Osteoarthritis project data analyses were undertaken using Stata version 14.1 at Oxford University. The remaining cohort analyses were undertaken in-house; Clinical Assessment Study of the Foot using Stata version 14 (Stata Corp, College Station, Texas, USA); Framingham Foot Study using SAS Version 9.4 (SAS Institute, Cary, NC); North West Adelaide Health Study using SPSS Version 24 (IBM, Armonk, NY, USA) and STATA 14.2 .

Ethics

The Chingford Women Study was approved by the Outer North East London Research Ethics Committee, and written consent was obtained from each woman. The Johnston County Osteoarthritis Project was approved by the Institutional Review Boards at the University of

North Carolina and the Centers for Disease Control and Prevention. Clinical Assessment Study of the Foot ethical approval was obtained from Coventry Research Ethics Committee (REC reference number: 10/ H1210/5) and all participants gave their written consent to participate. The Framingham Foot Study was approved by the Hebrew SeniorLife and Boston University Medical Center Institutional Review Boards and participants provided written, informed consent prior to enrolment. North West Adelaide Health Study ethical approval was obtained from the Human Research Ethics Committee of The Queen Elizabeth Hospital, Adelaide, South Australia and all participants provided written informed consent.

Results

Study population

A summary of sample characteristics of each cohort is shown in Table 1.

Response rates and loss to follow-up

Chingford Women Study

Of the original cohort of 1003 participants, 658 (65.6%) returned at year 15 in 2003 and completed a joint symptom questionnaire. Four (0.6% of year 15) participants were excluded from the current study due to missing data on foot pain, leaving 655 for analysis.

Johnston County Osteoarthritis Project

Of the original cohort of 3187 participants, 1739 (54.6%) returned for the follow-up clinic visit (T1) from 1999-2004. One hundred and twenty (6.9% of T1) participants were excluded from the current study due to missing data either in demographics or foot pain, leaving 1619 for analysis.

Clinical Assessment Study of the Foot

The baseline health survey questionnaire was mailed to 9334 adults and completed by 5109 (adjusted response 56%). Of these, 619 (12.1%) participants were excluded from the current study due to missing data either in the foot pain questions or demographics leaving 4,490 for analysis.

Framingham Foot Study

3429 participants were included in the baseline data collection between 2002 and 2008. Nine (0.3% of participants) were excluded from the current study due to missing data either in demographics or foot pain, leaving 3420 for analysis.

North West Adelaide Health Study

The original cohort of participants was 4056, with 3205 (79.0% of the eligible sample) participating in all three data collections (the CATI survey, self-complete questionnaire and clinic assessment) in Stage 2 between 2004 and 2006. Of these 60 (1.9% of stage 2 sample)

were excluded due to missing data either in the demographics or the foot pain questions, leaving 3145 for analysis.

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~~*Harmonisation*~~ *Standardisation of foot pain*

Each cohort was examined for available foot pain questions. Each cohort's foot pain questions were assessed for differences in the duration of pain (i.e. any/most days) and the period of recall (i.e. in the last month/last year/ever). As there was a variation of pain duration and recall between a number of the cohorts' questions, o~~O~~ne foot pain question was selected from each cohort based on its similarity to the American College of Rheumatology (ACR) question: "Have you had pain (in either foot) on most days in the last month?" [13].~~=~~ Where questions provided categorical answers these were standardised to provide dichotomous (yes/no) responses.

~~ach cohort's foot pain questions were assessed for differences in the duration of pain (i.e. any/most days) and the period of recall (i.e. in the last month/last year/ever). As there was a variation of pain duration and recall between a number of the cohorts' questions, a new harmonised pain variable was derived based on the common components of all questions; "Pain in either foot on most days"~~ (table 2).

The prevalence of foot pain ranged from 13 to 36% between cohorts (see Table 3 for all stratified foot pain results). Foot pain was more prevalent in women than men across all cohorts where data on both sexes were available, and the largest absolute difference in the occurrence of foot pain between men and women was 11% in the Framingham Foot Study. Prevalence ranged from 9-36% in those aged 55-64, 14-36% aged 65-74 and 15-37% in those

75 years and older (Figure 1). Foot pain was most prevalent in those classified as obese (BMI >30.0) in all cohorts (Figure 2). In the Johnston County Osteoarthritis Project, the Clinical Assessment Study of the Foot and the North West Adelaide Health Study, foot pain prevalence was also high at a BMI lower than 18.5, however numbers were small with wide 95% confidence intervals. Four cohorts reported race, two of which were limited to only Caucasian participants (Chingford Women Study and Framingham Foot Study). Prevalence of foot pain within Caucasian participants ranged from 13-36%. In the Johnston County Osteoarthritis Project, the frequency of foot pain was comparable in Caucasians and African Americans (36 and 35%, respectively). Where other races were available within the Clinical Assessment Study of the Foot, foot pain prevalence was highest amongst Africans at 38% compared to only 10% in Asian participants, however the number of these participants was low with wide confidence intervals.

Figure 1. ~~Prevalence of foot pain across cohorts by age~~

Figure 2. ~~Prevalence of foot pain across cohorts by BMI category~~

Discussion

This is the first study to use original data to compare the prevalence of foot pain across multiple international populations. Foot pain ranged from 13% in the Chingford Women Study, 18% in the North West Adelaide Health Study, 21% in the Clinical Assessment Study of the Foot, 25% in the Framingham Foot Study, to 36% in the Johnston County Osteoarthritis Project. The study highlights the differences in foot pain across age, sex, BMI

and race, whilst considering differences in case definitions used for variables, a vital consideration when combining or comparing data across multiple data sets.

Where cohorts included both men and women, there was a consistently higher prevalence of foot pain in women. This difference has been widely reported [6, 7, 9, 23], with a suggested partial attribution to lifetime footwear habits, although other factors such as occupation and family history are also thought to contribute [18, 24]. Women are more likely to report musculoskeletal pain in general and consideration should also be given to sex-related variations in pain perception [25] hormonal influences [26], and psychological and social factors [27]. However, the role of other potential sex differences such as occupation or physical activity levels is currently unknown. The overall prevalence of foot pain was actually lowest within the Chingford Women Study, the women-only cohort. Whilst unknown factors such as comorbidities may play a role, this is likely due to the case definition used for foot pain. In the Chingford Women Study the question was specific to pain only, in comparison to all other cohorts whose question included pain, aching and stiffness. This challenges whether the use of ~~pain~~ questions including aching and stiffness may overestimate pain. The original foot pain question in Chingford Women Study allowed for a categorical response of 0, 1-5, 6-14 and 15+ days. For the purposes of ~~harmonisation~~ standardising with the remaining four cohorts in this study, which all used a foot pain duration of "most days", a cut off of 15+ days was chosen to represent most days in the Chingford Women Study. This cut point was identical to that used in a previous study to represent painful knee osteoarthritis [28]. However, because no explicit number of days was provided to Chingford participants to represent "most" days, it cannot be assumed that all participants would classify 15+ days as most days. A sensitivity analysis was therefore

346 undertaken to estimate foot pain prevalence with an adjusted cut off point of 6+ days, to
347 capture participants who answered 6-14 days. Foot pain prevalence rose from 12.5% (15+
348 days) to 18% (6+ days), thus highlighting the sensitivity in prevalence estimates according to
349 the question response components.
350
351 The prevalence of foot pain generally increased with age and was much lower in younger
352 participants (20-44 years) compared to those over the age of 45 years. This increase is in
353 concordance with previous studies [7, 29]. Although small differences in foot pain
354 prevalence can be seen by decade above the age of 45, overlapping 95% confidence
355 intervals suggest there is little difference in these prevalence estimates. Results of a
356 systematic review and a survey study found a stronger positive association of foot pain with
357 age among women than men [7, 9]. This may ~~is likely~~ in part be ~~-~~due to ~~the~~gender
358 differences in pain perception, where women are known to report more severe levels of
359 pain, more frequent pain and pain of longer duration than do men [25, 27]. Also the higher
360 frequency of pain-related conditions ~~-~~such as osteoarthritis, which are seen more commonly
361 in women and older persons [30]. ~~and suggests that women of older age are more likely to~~
362 ~~report foot pain.~~
363
364 In all cohorts, the prevalence of foot pain was highest in those classified as obese. Foot pain
365 was more prevalent at the lower and upper extremes of BMI in the Johnston County
366 Osteoarthritis Project, the Clinical Assessment Study of the Foot and the North West
367 Adelaide Health Study, however small participant numbers and wide 95% confidence
368 intervals in the low BMI category (<18.5) suggest these estimates should be interpreted with
369 caution. Foot pain prevalence showed an incremental increase with BMI in the Framingham

Foot Study. Previous cross-sectional studies have also reported associations between increasing BMI and foot pain [31, 32], in particular fat mass [31, 33]. There is also evidence from longitudinal studies that BMI is a predictor of incident foot pain over 5 years [34] and fat mass is a predictor of incident foot pain over 3 years [35].

Race data were largely limited to the Caucasian demographic, with foot pain prevalence lower in both UK cohorts than the USA. In the bi-racial cohort of the Johnston County Osteoarthritis Project, the occurrence of foot pain was similar between Caucasians and African Americans. In the Clinical Assessment Study of the Foot, foot pain prevalence was highest in Africans, then Afro Caribbean and Caucasians of similar prevalence, and lowest in Asians, but interpretation of these findings is limited because only 2% of the sample were racial/ethnic minorities (not Caucasian). Previous studies found significant racial/ethnic differences in the prevalence of common foot disorders, independent of sex or education. Two previous studies, using data not included within the current study also found differences in between races. In the Feet First study, USA, the total number of foot conditions such as toe deformities, flat feet, corns, calluses and skin pathologies, and ankle joint pain were found to be more prevalent in African Americans than in non-Hispanic Whites and in Puerto Ricans [36]. In the Women's Health and Aging Study, USA, significant differences in pain severity were found between races, with more foot pain found in black than non-black participants [37].

It has been suggested that the differences in health conditions between racial and ethnic groups could be due to different levels of access to health care, different rates of chronic conditions (such as diabetes, obesity, or vascular disease) possibly associated with foot

ailments, early life experiences, or occupational patterns that differ among groups independently of education [36]. As ethnicity is the term given for the culture of people in a given geographical region, including but not limited to language, religion and customs, it would be beneficial to consider the role of ethnicity in the investigation of pain and/or conditions. Further work is required to determine the etiologic factors for such differences.

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~~The strengths of this study are that results are generalizable to first world populations, as data were sourced from population-based prospective observational cohorts at a time point where no enhancement was made for known risk factors, therefore reducing the chance of selection bias. This study analysed original cohort data and was therefore not limited to previously published data. Whilst most studies within standard meta-analysis use a variety of definitions of outcomes, the current study was able to minimise this variation by choosing similar questions at selected time points. This approach can be expanded to other time points and for other variables to enable longitudinal individual participant data meta-analysis to identify risk factors for foot pain and associated conditions. Although the wording of pain questions differed for two of the cohorts, all five cohorts used questions that were specific to self-reported foot pain.~~

The biggest challenge when comparing data across population cohorts is the heterogeneity that exists across factors such as recruitment methods, data collection time points and variable definitions. Even when comparable variable definitions are used, there is often further heterogeneity within the measures used to collect data and the parameters of each variable. The main limitation found from this study was the variation in questions used to determine the presence of foot pain, particularly the duration of pain and the question response components, as shown from the response categories in the original pain questions

in the Chingford Women Study. A recent study has shown that the variation of wording in NHANES type pain questions can result in varying knee pain prevalence between 41% and 75% [13]. Although the NHANEs type questions were designed to capture joint pain related to OA, we cannot confidently confirm the cause of foot pain in all participants.

The Chingford Women Study and the Framingham Foot Study are predominantly Caucasian, therefore results cannot be generalised to other races. Similarly, the Chingford Women Study is a woman-only cohort. Country of birth, but not race, was collected in the North West Adelaide Health Study. Those born in Australia were asked if they are Aboriginal or Torres Strait Islander (ATSI), however there were only 11 people who identified as ATSI in stage 2. Country of birth does not represent the race categories used in the remaining four cohorts. The North West Adelaide Health Study has a predominantly Caucasian sample and thus country of birth was not included in the analysis.

Johnston County, North Carolina is a ~~lower income,~~ semirural area in the southern US that includes a greater proportion of lower income residents than observed in the populations from which other cohorts in the present study were derived [38]. ~~An inverse relationship between~~ Foot pain frequency estimates for the Johnston County Osteoarthritis Project may be higher than other cohorts because lower socioeconomic status ~~and~~is associated with greater ~~the~~ [illegible] prevalence is likely high in the US, given that the cohort from Framingham, Massachusetts presents the second highest foot pain prevalence across these cohorts. Also, high BMI, which is also a ~~potentially important~~ factor associated with foot pain [34], is ~~highest~~more common in the Johnston County Osteoarthritis Project ~~participants~~ than in other cohorts.

Year 15 follow up was chosen in the Chingford Women Study due to the availability of a foot pain question at this time point. The inability to use baseline data resulted in a smaller sample than the original baseline. Those who did not attend year 15 tended to be older with a higher BMI at baseline compared to year 15 attendees who were selected for this study. For the Clinical Assessment Study of the Foot, response to the baseline health questionnaire was lower than expected (56%). However, responders did not differ greatly from the mailed population by age, sex or general practice [41]. For the Johnston County Osteoarthritis Project, generally persons who did not return for T1 tended to be older, less educated and more likely to be male and African American. For the North West Adelaide Health Study Stage 2 data collection was used for foot pain as this was the first time musculoskeletal questions were asked of the cohort. Participants who failed to provide information at stage 2 tended to be younger, with a slightly higher number of men than women.

The strengths of this study are that the results are based on data sourced from population-based prospective observational cohorts, therefore enhancing generalisability and reducing the chance of selection bias. This study analysed original participant data and was therefore not limited to the publication bias inherent with analysing previously published results. Whilst most studies within standard meta-analysis use a variety of definitions of outcomes, the current study was able to minimise this variation by choosing similar questions at selected time points. This approach can be expanded to other time points and for other variables to enable longitudinal individual participant data meta-analysis to identify risk factors for foot pain and associated conditions. Although the wording of pain questions

differed for two of the cohorts, all five cohorts used questions that were specific to self-reported foot pain.

This study provides useful comparisons of foot pain between five population cohorts. Comparisons show that irrespective of geographical location, the prevalence of foot pain is higher among those who are obese and lower in younger participants (20-44 years). Although lower in the younger population, it is important to recognise that foot pain does occur in this age-group and may warrant further investigation and clinical attention. Between-cohort data for race were limited, however within-cohort results showed foot pain was potentially more prevalent in African participants. Foot pain was also more prevalent in women than men.

This study has highlighted variation in how pain data is collected between cohorts. A degree of the variation in prevalence between cohorts may, at least in part, be due to the sensitivity of different pain definitions. In particular, it is important to consider the effect that including all the components of pain, aching or stiffness in one question may have on estimating the prevalence of pain only. Future population studies should use more consistent measures of data collection and the role of question response categories should not be underestimated. Agreement on a standardised set of key foot questions and measures would be useful for future prospective data collection phases within existing and newly establishing cohorts.

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Authors' contributions

All authors contributed to the planning of the manuscript. LSG, ABD, TKG and TRM completed the analysis. LSG collated results and cohort details and prepared the manuscript. All authors provided critical review of the paper, read and approved the final manuscript.

References

1. Peat G, Thomas E, Wilkie R, Croft P: **Multiple joint pain and lower extremity disability in middle and old age**. *Disability And Rehabilitation* 2006, **28**(24):1543-1549.
2. Menz HB, Morris ME, Lord SR: **Foot and ankle characteristics associated with impaired balance and functional ability in older people**. *Journals of Gerontology Series A: Biological Sciences & Medical Sciences* 2005, **60A**(12):1546-1552.
3. Menz HB, Morris ME, Lord SR: **Foot and ankle risk factors for falls in older people: a prospective study**. *Journals of Gerontology Series A: Biological Sciences & Medical Sciences* 2006, **61A**(8):866-870.
4. Mickle KJ, Munro BJ, Lord SR, Menz HB, Steele JR: **Foot pain, plantar pressures, and falls in older people: a prospective study**. *Journal of the American Geriatrics Society* 2010, **58**(10):1936-1940.
5. Mickle KJ, Munro BJ, Lord SR, Menz HB, Steele JR: **Cross-sectional analysis of foot function, functional ability, and health-related quality of life in older people with disabling foot pain**. *Arthritis Care Res (Hoboken)* 2011, **63**(11):1592-1598.
6. Hill C, Gill T, Menz H, 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**.
7. 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**(12):2870-2880.
8. 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**. *Journal of Foot and Ankle Research* 2016, **9**(1):23.
9. Garrow AP, Silman AJ, Macfarlane GJ: **The Cheshire foot pain and disability survey: a population survey assessing prevalence and associations**. *Pain* 2004, **110**.
10. Menz HB, Jordan KP, Roddy E, Croft PR: **Characteristics of primary care consultations for musculoskeletal foot and ankle problems in the UK**. *Rheumatology (Oxford, England)* 2010, **49**(7):1391-1398.
11. Menz HB, Jordan KP, Roddy E, Croft PR: **Musculoskeletal foot problems in primary care: what influences older people to consult?** *Rheumatology (Oxford, England)* 2010, **49**(11):2109-2116.
12. Tierney JF, Vale C, Riley R, Smith CT, Stewart L, Clarke M, Rovers M: **Individual Participant Data (IPD) Meta-analyses of Randomised Controlled Trials: Guidance on Their Use**. *PLoS Medicine* 2015, **12**(7):e1001855.
13. Leyland KM, Gates LS, Nevitt M, Felson D, Bierma-Zeinstra SM, Conaghan PG, Engebretsen L, Hochberg M, Hunter DJ, Jones G *et al*: **Harmonising measures of knee and hip osteoarthritis in population-based cohort studies: an international study**. *Osteoarthritis Cartilage* 2018.
14. Gates LS, Leyland KM, Sheard S, Jackson K, Kelly P, Callahan LF, Pate R, Roos EM, Ainsworth B, Cooper C *et al*: **Physical activity and osteoarthritis: a consensus study to harmonise self-reporting methods of physical activity across international cohorts**. *Rheumatology International* 2017, **37**(4):469-478.
15. Hart DJ, Spector TD: **The relationship of obesity, fat distribution and osteoarthritis in women in the general population: the Chingford Study**. *J Rheumatol* 1993, **20**(2):331-335.
16. Jordan JM: **An Ongoing Assessment of Osteoarthritis in African Americans and Caucasians in North Carolina: The Johnston County Osteoarthritis Project**. *Transactions of the American Clinical and Climatological Association* 2015, **126**:77-86.
17. Roddy E, Myers H, Thomas MJ, Marshall M, D'Cruz D, Menz HB, Belcher J, Muller S, Peat G: **The clinical assessment study of the foot (CASF): study protocol for a prospective observational study of foot pain and foot osteoarthritis in the general population**. *Journal of Foot and Ankle Research* 2011, **4**(1):22.
18. Dufour AB, Broe KE, Nguyen US, Gagnon DR, Hillstrom HJ, Walker AH: **Foot pain: is current or past shoewear a factor?** *Arthritis Rheum* 2009, **61**.
19. Grant JF, Taylor AW, Ruffin RE, Wilson DH, Phillips PJ, Adams RJ: **Cohort profile: The North West Adelaide Health Study (NWAHS)**. *Int J Epidemiol* 2009, **38**.
20. Dawber TR, Meadors GF, Moore FE: **Epidemiological Approaches to Heart Disease: The Framingham Study**. *American Journal of Public Health and the Nations Health* 1951, **41**(3):279-286.

21. Feinleib M, Kannel WB, Garrison RJ, McNamara PM, Castelli WP: **The Framingham Offspring Study. Design and preliminary data.** *Preventative Medicine* 1975, **4**:518-525.
22. Grant JF, Chittleborough CR, Taylor AW, Dal Grande E, Wilson DH, Phillips PJ: **The North West Adelaide Health Study: detailed methods and baseline segmentation of a cohort for selected chronic diseases**. *Epidemiol Perspect Innov* 2006, **3**.
23. Thomas E, Peat G, Harris L, Wilkie R, Croft PR: **The prevalence of pain and pain interference in a general population of older adults: cross-sectional findings from the North Staffordshire Osteoarthritis Project (NorStOP)**. *Pain* 2004, **110**(1-2):361-368.
24. Dawson J, Thorogood M, Marks SA, Juszczak E, Dodd C, Lavis G, Fitzpatrick R: **The prevalence of foot problems in older women: a cause for concern**. *Journal of public health medicine* 2002, **24**(2):77-84.
25. Unruh AM: **Gender variations in clinical pain experience**. *Pain* 1996, **65**(2-3):123-167.
26. Fillingim RB, Ness TJ: **Sex-related hormonal influences on pain and analgesic responses**. *Neuroscience and biobehavioral reviews* 2000, **24**(4):485-501.
27. Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL, 3rd: **Sex, gender, and pain: a review of recent clinical and experimental findings**. *The journal of pain : official journal of the American Pain Society* 2009, **10**(5):447-485.
28. Kluzek S, Sanchez-Santos MT, Leyland KM, Judge A, Spector TD, Hart D, Cooper C, Newton J, Arden NK: **Painful knee but not hand osteoarthritis is an independent predictor of mortality over 23 years follow-up of a population-based cohort of middle-aged women**. *Ann Rheum Dis* 2016, **75**(10):1749-1756.
29. Thomas E, Peat G, Harris L, Wilkie R, Croft PR: **The prevalence of pain and pain interference in a general population of older adults: cross-sectional findings from the North Staffordshire Osteoarthritis Project (NorStOP)**. *Pain* 2004, **110**.
30. Blagojevic M, Jinks C, Jeffery A, Jordan KP: **Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis**. *Osteoarthritis and Cartilage* 2010, **18**(1):24-33.
31. Tanamas SK, Wluka AE, Berry P, Menz HB, Strauss BJ, Davies-Tuck M: **Relationship between obesity and foot pain and its association with fat mass, fat distribution, and muscle mass**. *Arthritis Care Res* 2012, **64**.
32. 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**.
33. Butterworth PA, Menz HB, Urquhart DM, Cicuttini FM, Landorf KB, Pasco JA: **Fat mass is associated with foot pain in men**. *J Rheumatol* 2016, **43**.
34. Gay A, Culliford D, Leyland K, Arden NK, Bowen CJ: **Associations between body mass index and foot joint pain in middle-aged and older women: A longitudinal population-based study**. *Arthritis Care Res* 2014, **66**.
35. Butterworth PA, Urquhart DM, Cicuttini FM, Menz HB, Strauss BJ, Proietto J, Dixon JB, Jones G, Landorf KB, Wluka AE: **Fat mass is a predictor of incident foot pain**. *Obesity (Silver Spring, Md)* 2013, **21**(9):E495-499.
36. Dunn J, Link C, Felson D, Crincoli MG, Keysor JJ, McKinlay JB: **Prevalence of foot and ankle conditions in a multiethnic community sample of older adults**. *Am J Epidemiol* 2004, **159**.
37. Leveille SG, Guralnik JM, Ferrucci L, Hirsch R, Simonsick E, Hochberg MC: **Foot pain and disability in older women**. *American Journal of Epidemiology* 1998, **148**.
38. Qin J, Barbour KE, Murphy LB, Nelson AE, Schwartz TA, Helmick CG, Allen KD, Renner JB, Baker NA, Jordan JM: **Lifetime Risk of Symptomatic Hand Osteoarthritis: The Johnston County Osteoarthritis Project**. *Arthritis & rheumatology (Hoboken, NJ)* 2017, **69**(6):1204-1212.
39. McBeth J, Jones K: **Epidemiology of chronic musculoskeletal pain**. *Best Pract Res Clin Rheumatol* 2007, **21**(3):403-425.
40. Dorner TE, Muckenhuber J, Stronegger WJ, Rasky E, Gustorff B, Freidl W: **The impact of socio-economic status on pain and the perception of disability due to pain**. *European journal of pain (London, England)* 2011, **15**(1):103-109.
41. Roddy E, Thomas MJ, Marshall M, Rathod T, Myers H, Menz HB, Thomas E, Peat G: **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**(1):156-163.

Table 1. Demographic characteristics of each cohort

		Chingford Women	**Johnston County Osteoarthritis Project**	**Framingham Foot Study**	**Clinical Assessment Study of the Foot**	**North West Adelaide Health Study**
Data collection time point		Year 15 (2003)	T1 (1999-2004)	Phase 1 (2002 and 2008)	Respondents to baseline health survey (2010-2011)	Participants at stage 2 clinic (2004–2006)
n (at time point)		655	1619	3420	4490	3145
Age, M (± SD y)		68.6 (5.8)	65.8 (9.8)	66.5 (10.6)	64.9 (9.8)	47.6 (17.5)
Age category, n (%)	20–34	-	-	-	-	889 (28.3)
	35–44	-	-	17 (0.5)	-	644 (20.5)
	45–54	-	203 (12.5)	451 (13.2)	741 (16.5)	557 (17.7)
	55–64	206 (31.5)	592 (36.6)	1208 (35.3)	1624 (36.2)	428 (13.6)
	65–74	308 (47.0)	484 (29.9)	944 (27.6)	1334 (29.7)	320 (10.2)
	≥75	141 (21.5)	340 (21.0)	800 (23.4)	791 (17.6)	307 (9.8)
Sex	Men, n (%)	-	581 (35.9)	1499 (43.8)	2198 (49.0)	1545 (49.1)
	Women, n (%)	655 (100.0)	1038 (64.1)	1921 (56.2)	2292 (51.0)	1600 (50.9)
Body mass index, M ± SD kg/m2		27.2 (4.8)	30.2 (6.3)	28.4 (5.5)	27.5 (5.2)	27.8 (5.7)
Body mass index category, n (%)	<18.5	10 (1.5)	13 (0.8)	23 (0.7)	62 (1.4)	43 (1.4)
	18.5–24.9	228 (34.8)	290 (17.9)	937 (27.4)	1480 (33.0)	1014 (32.2)
	25.0–29.9	241 (36.8)	588 (36.3)	1335 (39.0)	1808 (40.3)	1169 (37.2)
	≥30.0	176 (26.9)	728 (45.0)	1125 (32.9)	1140 (25.4)	919 (29.2)

Prevalence of foot pain across cohorts

Race	Caucasian, n (%)	655 (100.0)	1158 (71.5)	3420 (100.0)	4395 (97.9)	-
	African American, n (%)		461 (28.5)	-	-	-
	Afro Caribbean, n (%)		-	-	14 (0.3)	-
	Asian, n (%)		-	-	49 (1.1)	-
	African, n (%)		-	-	8 (0.2)	-
	Other, n (%)		-	-	24 (0.5)	-

Table 2. Harmonisation of foot pain variable across cohorts

Cohort	Original Question	~~Transformed~~ Responses standardised to match "pain on most day" ~~variable~~
Chingford Women Study	"On how many days[§] in the last month* did you get pain?" (0/1-5/6-14/15+ days) [§]	Pain in either foot on most days (L/R) 1. Pain on most days (yes)= pain on at least 15 days 2. Pain on most days (no) = pain on less than 15 days
Johnston County Osteoarthritis Project	"On most days[§] do you have pain, aching or stiffness in your feet?" (Yes/No)	Pain in either foot on most days (L/R) 1. Yes 2. No
Framingham Foot Study	"On most days[§] do you have pain, aching or stiffness in your feet?" (Yes/No)	Pain in either foot on most days (L/R) 1. Yes 2. No
Clinical Assessment Study of the Foot	"Pain, aching or stiffness in the foot in the past month*" (No days/Few days/Some days/Most days/All days)[§]	Pain in either foot on most days (L/R) 1. Pain on most days (yes)= Most days/All days & had foot pain in the last year 2. Pain on most days (no) = No days/Few days/Some days & had foot pain in the last year OR did not have foot pain in the last year
North West Adelaide Health Study	"On most days[§], do you have pain, aching or stiffness in either of your feet?" (Yes/No)	Pain in either foot on most days (L/R) 1. Yes 2. No

*Period of recall for foot pain [§]Duration of foot pain

Prevalence of foot pain across cohorts

Table 3. Prevalence of foot pain stratified by age, sex, body mass index (BMI) and race

		Chingford 1000 Women	**Johnston County Osteoarthritis Project**	**Framingham Foot Study**	**Clinical Assessment Study of the Foot**	**North West Adelaide Health Study**
		N=665	N=1619	N=3420	N=4490	N=555
Foot pain % (95% CI)		12.5 (10.2, 15.3)	36.0 (33.7, 38.4)	25.0 (23.5, 26.4)	20.6 (19.5, 21.8)	17.7 (16.0-19.4)
Age % (95% CI)	20–34		-	-	-	10.5 (7.0-15.4)
	35–44		-	11.8 (0.0, 28.8)	-	10.8 (8.4-13.8)
	45–54		34.5 (28.2, 41.3)	28.2 (24.0, 32.3)	19.6 (16.9, 22.6)	21.8 (18.5-25.4)
	55–64	9.2 (5.9, 14.1)	36.0 (32.2, 39.9)	26.6 (24.1, 29.1)	20.5 (18.6, 22.5)	24.2 (20.8-28.0)
	65–74	13.6 (10.2, 18.0)	35.7 (31.6, 40.1)	22.4 (19.7, 25.0)	20.3 (18.2, 22.6)	26.4 (22.5-30.8)
	75≥	14.9 (9.9, 21.9)	37.4 (32.4, 42.7)	24.1 (21.2, 27.1)	22.4 (19.6, 25.4)	27.0 (22.4-32.2)
Sex % (95% CI)	Men		30.5 (26.9, 34.3)	19.0 (17.0, 21.0)	18.3 (16.7, 20.0)	15.3 (13.2-17.7)
	Women	12.5 (10.2, 15.3)	39.1 (36.2, 42.1)	29.6 (27.6, 31.7)	22.9 (21.2, 24.6)	19.9 (17.5-22.5)
BMI (kg/m^2) % (95% CI)	<18.5	10.0 (0.8, 57.8)	38.5 (14.6, 69.5)	17.4 (0.6, 34.2)	22.6 (13.7, 35.0)	22.3 (6.4-54.8)
	18.5 – 24.9	11.4 (7.9, 16.3)	26.6 (21.8, 32.0)	20.7 (18.1, 23.3)	14.4 (12.7, 16.3)	10.8 (8.7-13.2)
	25.0 – 29.9	10.0 (6.7, 14.5)	31.0 (27.3, 34.8)	22.8 (20.5, 25.0)	19.1 (17.4, 21.0)	17.6 (15.3-20.2)

Prevalence of foot pain across cohorts

	30.0≥	17.6 (12.6, 24.0)	43.8 (40.2, 47.5)	31.3 (28.6, 34.0)	31.0 (28.3, 33.7)	25.1 (21.6-29.0)
	Caucasian	12.5 (10.2, 15.3)	36.4 (33.7, 39.3)	25.0 (23.5, 26.4)	20.8 (19.6, 22.0)	-
	African American	-	34.9 (30.7, 39.4)	-	-	-
Race %	Afro					
(95% CI)	Caribbean	-	-	-	21.4 (6.0, 54.0)	-
	Asian	-	-	-	10.2 (4.2, 22.9)	-
	African	-	-	-	37.5 (8.7, 79.2)	-
	Other	-	-	-	12.5 (3.7, 34.5)	-