Prevalence of Reported Knee Pain Over Twelve Years in a Community-Based Cohort

A. Soni,1 A. Kiran,1 D. J. Hart,2 K. M. Leyland,1 L. Goulston,3 C. Cooper,4 M. K. Javaid,1 T. D. Spector,2 and N. K. Arden4

Objective. To describe the temporal patterns of knee pain in a community-based cohort over 12 years.

Methods. Data on self-reported knee pain at 4 time points over 12 years were analyzed in participants from the Chingford Women’s Study of osteoarthritis (OA) and osteoporosis. Pain status was defined as any pain in the preceding month and pain on most days in the preceding month. This status was used to classify participants according to pain patterns of asymptomatic, persistent, incident, or intermittent pain. Multinomial logistic regression was used to identify baseline predictors for each pain pattern.

Results. Among the 489 women with complete followup data, the median age at baseline was 52 years (interquartile range [IQR] 48–58 years), the median body mass index (BMI) was 24.39 kg/m² (IQR 22.46–27.20), and 11.7% of the women had a Kellgren/Lawrence radiographic OA severity grade of ≥2 in at least one knee. Among subjects reporting any pain in the preceding month versus those reporting pain on most days in the preceding month, 9% versus 2% had persistent pain, 24% versus 16% had incident pain, and 29% versus 18% had intermittent pain. A higher BMI was predictive of persistent pain (odds ratio [OR] 1.14, 95% confidence interval [95% CI] 1.04–1.25) and incident pain (OR 1.10, 95% CI 1.02–1.18). The presence of radiographic knee OA was predictive of persistent pain (OR 3.70, 95% CI 1.34–10.28; P = 0.012), and reported knee injury was predictive of both persistent pain (OR 4.13, 95% CI 1.34–12.66; P = 0.013) and intermittent pain (OR 4.25, 95% CI 1.81–9.98; P = 0.001).

Conclusion. Significant variability in the temporal fluctuation of self-reported knee pain was seen in this community-based prospective study over a period of 12 years, with few women consistently reporting knee pain at each time point. Distinct baseline predictors for each pain pattern were identified and may explain the observed heterogeneity of self-reported knee pain when pain status is measured at only one time point.

Osteoarthritis (OA) is a leading cause of worldwide disability, with an estimated annual loss of productivity cost of £3.2 billion in the UK, with pain being the most troublesome symptom experienced by patients (1). In particular, knee OA is associated with persistent impairment of physical function and substantial societal burden (2,3). Determining risk factors for both the onset and progression of knee pain is required to further the development of targeted therapeutic strategies and to plan future healthcare service provision. Although knee pain does not always equate to radiographic OA (4,5), the importance of conducting more detailed assessments of symptoms has been reported (6), and longitudinal studies are now beginning to focus on predictors of poor patient-reported outcomes, including severity of pain and disability (7,8), rather than radiographic progression.

It has also been noted that pain perception is not linearly related to the severity of peripheral noxious input but is critically influenced by higher central affec-
tive and cognitive features, which vary substantially between individuals (9). Hence, even weak sensory inputs can elicit significantly painful sensations, and conversely, stronger stimuli may not yield a painful sensation in some subjects, depending on the individual’s susceptibility to pain (10). The corresponding heterogeneity of pain experienced by patients with knee OA is being increasingly recognized as more comprehensive pain assessment methods are utilized, and it is anticipated that improved measurement of pain will result in better understanding of pain mechanisms in OA, enabling targeted treatment decisions (11–14).

One aspect of pain is its temporal fluctuation, being defined as a state of either intermittent pain or persistent pain, which may inform insights into etiologic mechanisms. The importance of intermittent symptoms was highlighted recently by a study in which a substantial proportion of subjects demonstrated inconsistent knee pain over ~1 month, in whom a number of distinguishing risk factors were identified when compared to subjects whose knee pain was consistent (14). Our primary objective in the present study was to describe the prevalence, natural history, and predictors of knee pain in a community-based cohort over 12 years, utilizing data from several time points to describe fluctuations in patients’ self-reported pain.

PATIENTS AND METHODS

Setting and subjects. The study participants were selected from the Chingford Women’s Study, a well-described prospective, population-based longitudinal study of OA and osteoporosis, comprising 1,003 women derived from the register of a large general practice in Chingford, North London, UK (15,16). The women, ages 44–67 years, are representative of women in the UK general population with respect to weight, height, and smoking characteristics (16). The study was established in 1989, and at year 15 of the study, 654 women remained, 111 women had died, 21 were incapacitated, and 217 were lost to followup. The study was approved by the local ethics committee, and written consent was obtained from each woman, in accordance with the Declaration of Helsinki.

At baseline, alcohol consumption, smoking habits, physical activity, and a history of knee injury were ascertained using a nurse-administered questionnaire. Dolorimetry measurements of the forehead and height and weight were made, and full-extension radiographs of the knees were obtained and graded for structural features of OA using the Kellgren/Lawrence (K/L) scoring system (17), on a 4-point scale. For the purpose of this study, the presence of radiographic OA was defined as a K/L radiographic severity grade of ≥2. Further annual assessments captured information regarding subsequent knee replacement surgery, which was validated with corresponding general practitioner documentation.

Knee pain assessment. Data on self-reported knee pain were collected using two questions. First, patients were asked, “Have you had any knee pain in either knee in the last month?” Second, patients were asked, “How many days of pain have you experienced in the last month?” Subjects were classified as having any knee pain if they responded “yes” to the question of having any knee pain in the preceding month.

The analysis was then repeated with the pain status being defined as the presence of knee pain on most days of the preceding month, consistent with the criteria of the First National Health and Nutrition Examination Survey (18). Since the knee pain data ascertained in years 3, 5, 6, 10, and 15 were consistent, the data from year 3 were therefore selected as a surrogate baseline for this substudy, while the data from year 6 were discounted in order to preserve approximately equal intervals between time points. Subjects who underwent total knee replacement were classified as having a positive pain status thereafter (3 subjects in the cohort reporting any knee pain in the preceding month, and 7 subjects reporting knee pain on most days of the preceding month).

Statistical analysis. In order to describe the temporal pattern of knee pain at the individual level, we focused on the subgroup of subjects who had a complete response to the knee pain questions at years 3, 5, 10, and 15; hereafter, this subgroup is referred to as the attendee cohort. The baseline demographic data for the attendee cohort were compared to the data for those subjects excluded due to incomplete data, using the Wilcoxon–Mann-Whitney test for non-normal continuous data and the chi-square test for categorical data.

For each subject, the pain status at each visit was determined. Based on this status, each patient was classified a priori according to pain patterns of asymptomatic (no pain at any time point), persistent (pain present at each visit), incident (no pain at baseline, but developed pain at any followup visit, which persisted until the year 15 visit, or new-onset pain at the year 15 visit alone), and intermittent (presence of pain and no pain, which did not meet the criteria for incident pain). Multinomial logistic regression was performed to identify baseline predictors for each pain pattern. Potential confounders were also chosen a priori, with the reference group being asymptomatic subjects. A sensitivity analysis was also performed to assess a more inclusive cohort, comprising subjects for whom complete pain data were available at year 3 and at least 2 other followup visits (n = 759).

All statistical analyses were performed using the R program, version 2.9.1 (2009-06-26), Stata SE version 10 (StataCorp), and Matlab R2009b (MathWorks).

RESULTS

Of 1,003 participants enrolled in the Chingford Women’s Study, 489 were included in the attendee cohort. Baseline demographics for these subjects and for the subjects excluded due to incomplete data are shown in Table 1. There were small, but statistically significant, differences in the attendee cohort compared to the excluded cohort, with the attendee cohort having a lower mean age (P < 0.001), a lower percentage of subjects...
reporting any days of knee pain at baseline for the left knee (19.84% versus 26.82%; \( P = 0.014 \)) and for the right knee (21.88% versus 28.43%; \( P = 0.025 \)), and lower body mass index (BMI) (24.39 kg/m² versus 25.23 kg/m²; \( P = 0.002 \)). The attendee cohort also had a lower frequency of radiographic OA, defined as a K/L grade \( \geq 2 \), compared to the excluded cohort.

The prevalence of knee pain in the attendee cohort over time is shown in Figure 1. The prevalence at year 15 was 43.8% (214 of 489 patients) for those reporting a status of any days of pain, and 22.9% (112 of 489 patients) for those reporting a status of pain on most days of the preceding month.

The prevalence of any knee pain in the preceding month and for most days of the preceding month in those with and those without reported knee pain at baseline (the year 3 visit) is shown in Figures 2A and B. As anticipated, those without knee pain at baseline had an increase in pain prevalence with duration of followup, with a prevalence at year 15 of 35.2% for those reporting any days of pain (Figure 2A) and 19.8% for those reporting most days of pain (Figure 2B) in the preceding month. While subjects with any knee pain at baseline had a higher prevalence of knee pain at all subsequent time points when compared to those without knee pain at baseline, a sizable minority of the subjects with pain at...
baseline no longer reported any knee pain at the respective followup visits at year 5 (39.0%), year 10 (43.1%), and year 15 (30.9%). Among those subjects reporting knee pain on most days of the preceding month, for those with pain at baseline, 68.0% at year 5, 56.0% at year 10, and 50.0% at year 15 no longer reported this pain status.

Figures 3A and B demonstrate the temporal pattern of knee pain over the 12-year period. Among subjects with any pain in the preceding month, 9% experienced persistent pain, 24% reported incident pain, and 29% experienced intermittent pain. Among subjects with pain on most days of the preceding month, 2% reported persistent pain, 16% reported incident pain, and 18% had intermittent pain.

We then examined determinants of the patterns of knee pain, using multinomial logistic regression analyses (Table 2). In the univariate model, for the group of subjects reporting any days of pain, age was a significant predictor of persistent pain ($P = 0.024$), but was not associated with any of the other patterns of pain. However, in the multivariate model, age was no longer a significant predictor of any of the pain patterns. In addition, baseline BMI, K/L grade, and previous knee injury were significant predictors of persistent knee pain ($P < 0.05$) in both the univariate model and the multivariate model. BMI was also predictive of incident knee pain in both models, while previous knee injury was a significant predictor of intermittent knee pain in both models.

For the group of subjects reporting pain on most days of the preceding month, the sample size of the

Figure 2. Prevalence of knee pain at each time point according to baseline (year 3) self-reported pain status of no pain versus A, any days with pain or B, pain on most days in the preceding month. Bars show the means with 95% confidence intervals.

Figure 3. Classification of pain over time among women in the attendee cohort, according to pain status of A, any days with pain or B, pain on most days in the preceding month. Bars show the mean.
A group with persistent pain was too small (n = 6) to derive statistical associations. Among the subjects reporting pain on most days, BMI at baseline was a significant predictor of both incident pain and intermittent pain in the univariate model, and was a significant predictor of incident pain in the multivariate model. Previous knee injury was predictive of intermittent pain in both the univariate model and the multivariate model.

An additional sensitivity analysis was performed to assess a more inclusive cohort, comprising subjects for whom complete pain data were available for year 3 and at least 2 other visits (Table 3). With the larger sample size of this subset (n = 759 women), the proportions of subjects in each pain pattern group remained very similar to those in the complete cohort. For the pain status of any days of pain, 6% of subjects reported persistent pain, 23% reported incident pain, and 33% reported intermittent pain, compared to 9%, 24%, and 29%, respectively, in the whole cohort, with only the proportion of subjects with intermittent pain being statistically significantly different from that in the whole cohort (P = 0.01). For the pain status of pain on most days, there were no statistically significant changes in the distribution of pain patterns, with 1%, 14%, and 19% of subjects reporting persistent pain, incident pain, and intermittent pain, respectively, compared to 2%, 16%, and 18%, respectively, in the complete cohort.

For subjects in this subset who reported any days of knee pain, both previous knee injury and the K/L radiographic severity grade (K/L grade < 2 versus ≥ 2) were significant predictors for all pain pattern classes in both the univariate model and the multivariate model.

### Table 2. Multinomial logistic regression analyses assessing baseline univariate/multivariate predictors of pain according to classification of pain pattern over time, among all participants*

<table>
<thead>
<tr>
<th>Pain status, model, predictor</th>
<th>Persistent pain (n = 45)</th>
<th>Incident pain (n = 118)</th>
<th>Intermittent pain (n = 144)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Any pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Univariate model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (in years) at year 1</td>
<td>1.06 (1.01–1.12)</td>
<td>0.024</td>
<td>1.02 (0.97–1.06)</td>
</tr>
<tr>
<td>BMI (in kg/m²) at year 1</td>
<td>1.18 (1.09–1.28)</td>
<td>&lt;0.001</td>
<td>1.11 (1.03–1.18)</td>
</tr>
<tr>
<td>K/L grade at year 1</td>
<td>7.85 (3.28–18.80)</td>
<td>&lt;0.001</td>
<td>2.41 (1.07–5.39)</td>
</tr>
<tr>
<td>Knee injury prior to year 1</td>
<td>6.00 (2.14–16.81)</td>
<td>0.001</td>
<td>2.44 (0.95–6.31)</td>
</tr>
<tr>
<td>Dolorimetry measurement (in kg/cm²)</td>
<td>0.64 (0.43–0.97)</td>
<td>0.036</td>
<td>0.88 (0.66–1.16)</td>
</tr>
<tr>
<td>Physical activity score (scale 0–12)</td>
<td>0.96 (0.77–1.18)</td>
<td>0.680</td>
<td>1.02 (0.87–1.20)</td>
</tr>
<tr>
<td>Fibromyalgia widespread pain</td>
<td>1.60 (0.30–8.55)</td>
<td>0.583</td>
<td>0.60 (0.11–3.15)</td>
</tr>
<tr>
<td>Multivariate model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (in years) at year 1</td>
<td>1.04 (0.98–1.10)</td>
<td>0.177</td>
<td>1.00 (0.95–1.04)</td>
</tr>
<tr>
<td>+ BMI (in kg/m²) at year 1</td>
<td>1.14 (1.04–1.25)</td>
<td>0.003</td>
<td>1.10 (1.02–1.18)</td>
</tr>
<tr>
<td>+ K/L grade at year 1</td>
<td>3.70 (1.34–10.28)</td>
<td>0.012</td>
<td>1.38 (0.55–3.47)</td>
</tr>
<tr>
<td>+ Knee injury prior to year 1</td>
<td>4.13 (1.34–12.66)</td>
<td>0.013</td>
<td>2.23 (0.86–5.76)</td>
</tr>
<tr>
<td>Pain on most days of the preceding month</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Univariate model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (in years) at year 1</td>
<td>1.00 (0.96–1.05)</td>
<td>0.969</td>
<td>1.00 (0.96–1.04)</td>
</tr>
<tr>
<td>BMI (in kg/m²) at year 1</td>
<td>1.12 (1.05–1.20)</td>
<td>&lt;0.001</td>
<td>1.08 (1.02–1.16)</td>
</tr>
<tr>
<td>K/L grade at year 1</td>
<td>1.35 (0.61–3.00)</td>
<td>0.459</td>
<td>2.37 (1.21–4.64)</td>
</tr>
<tr>
<td>Knee injury prior to year 1</td>
<td>1.12 (0.46–2.69)</td>
<td>0.807</td>
<td>2.39 (1.19–4.79)</td>
</tr>
<tr>
<td>Dolorimetry measurement (in kg/cm²)</td>
<td>0.82 (0.60–1.11)</td>
<td>0.213</td>
<td>0.80 (0.58–1.07)</td>
</tr>
<tr>
<td>Physical activity score (scale 0–12)</td>
<td>1.06 (0.89–1.25)</td>
<td>0.524</td>
<td>1.03 (0.89–1.20)</td>
</tr>
<tr>
<td>Fibromyalgia widespread pain</td>
<td>0.97 (0.20–4.68)</td>
<td>0.973</td>
<td>2.74 (0.92–8.12)</td>
</tr>
<tr>
<td>Multivariate model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (in years) at year 1</td>
<td>0.99 (0.94–1.04)</td>
<td>0.652</td>
<td>0.99 (0.95–1.04)</td>
</tr>
<tr>
<td>+ BMI (in kg/m²) at year 1</td>
<td>1.12 (1.04–1.19)</td>
<td>0.002</td>
<td>1.06 (1.00–1.14)</td>
</tr>
<tr>
<td>+ K/L grade at year 1</td>
<td>1.09 (0.43–2.72)</td>
<td>0.859</td>
<td>2.12 (0.94–4.79)</td>
</tr>
<tr>
<td>+ Knee injury prior to year 1</td>
<td>1.05 (0.43–2.58)</td>
<td>0.907</td>
<td>2.15 (1.04–4.45)</td>
</tr>
</tbody>
</table>

* The reference group for determination of odds ratios (ORs) comprised all asymptomatic subjects. The Kellgren/Lawrence (K/L) grade was dichotomized as grade 0–1 versus grade ≥2 (highest grade from each patient’s left knee and right knee). Knee injury and fibromyalgia widespread pain were dichotomized as present versus absent. 95% CI = 95% confidence interval; BMI = body mass index.
† Data were not available (NA) because the sample size was too small to derive statistical associations.
with stronger effects for those with persistent pain compared to those with either incident pain or intermittent pain (Table 3). In the multivariate model, increasing BMI remained a significant independent predictor in the persistent pain and incident pain groups, whereas age was not a predictor in any pain group. For subjects in this subset who reported pain on most days of the preceding month, the dolorimetry score became significant in the univariate model, but not in the multivariate model, and a higher K/L grade was a predictor of intermittent pain in both the crude and adjusted models.

**DISCUSSION**

This study demonstrates that knee pain is a commonly reported symptom in this community-based cohort; by year 15, 62.8% of the subjects had experienced any days of knee pain at least once in one knee. The presence of pain at baseline was predictive of a significantly higher risk of subsequent knee pain, but at any particular time point, up to 43.1% of the subjects did not subsequently report having knee pain. The specific time course of knee pain varied among individuals over the 12-year period, with 9% reporting persistent pain, 24% reporting incident knee pain, and 29% experiencing intermittent pain. Baseline predictors for persistent pain included BMI, K/L grade, and previous knee injury.

To our knowledge, no other community-based studies have described longitudinal patterns of knee pain and incorporated assessments from more than 2 time points over more than 10 years. A clinically significant improvement, but not complete resolution, of the symptoms from knee OA has been reported in 27% of individuals followed up for 7 years (7), which roughly corresponds to our results with regard to reported...
intermittent pain over time. In a cross-sectional survey of individuals older than age 65 years in Oxfordshire, UK, investigators observed a knee pain prevalence of 36.2% among women between the ages of 65 years and 74 years (19). Similarly, a survey of individuals from North Staffordshire, UK revealed that the 12-month prevalence of knee pain was 49% among women with a mean age of 65.4 years (20). In our younger cohort of women, the baseline (year 3) prevalence of any knee pain was only 25.6% (123 of 489 subjects).

This study highlights the value of the temporal pattern of pain, even when using quinquennial assessments, in identifying different subgroups of pain and may explain the heterogeneity of findings in the literature when pain is measured at only one time point. Although the sample size was small, those with persisting pain were significantly more likely to have a higher BMI, to have radiographic OA, and to have a history of knee injury. Although the incident and intermittent pain groups were of a similar sample size, their predictors differed, with higher BMI being a risk factor for incident pain and reported knee injury being a risk factor for intermittent pain.

These findings add to those of a study by Neogi et al that focused on consistency of knee pain symptoms over ~1 month, in which 43% of patients demonstrated inconsistent knee pain and 57% had consistent knee pain (14). Subjects with radiographic OA, symptoms of depression, and widespread pain were less likely to have inconsistent pain, whereas pain severity, function, and quadriceps strength were significantly better in those with inconsistent pain. Older patients were also more likely to have inconsistent knee pain. Moreover, the findings for K/L grade matched the results in our study, despite the very different duration of followup; however, we were unable to demonstrate a meaningful association with age, which may be due to the narrow age range in our cohort. Conversely, our study identified BMI as a significant predictor of pain of a more consistent nature, raising the possibility of an effect of BMI on the persistence of pain perception.

Numerous factors have been proposed as possible explanations for the apparent discordance between the presence of radiographic knee OA and corresponding pain, including the definition of pain used (4,21,22). This study emphasizes the importance of considering the temporal pattern of pain over several years, giving rise to the finding that baseline K/L grade acts as a predictor only in subjects whose pain is persistent over time and is not a significant factor in those with incident or intermittent pain.

One of the main strengths of this study is the fact that it describes the natural history of knee pain over 12 years, incorporating data from multiple time points. Pain data have been collected prospectively, circumventing the effect of recall bias. The study is also based on a large community-based cohort with excellent response and detainment rates, with the participating women being representative of those in the general UK population. Because we performed complete case analyses, there was a selection bias toward younger female subjects, whose BMI was lower and fewer of whom had knee pain and radiographic OA at baseline. The study is therefore likely to have underestimated the overall prevalence of knee pain in the community and also underestimated the occurrence of incident and persistent pain. As an attempt to address this bias, we included all subjects for whom there were complete data for the year 3 visit and at least 2 other followup visits (an expanded case sample). While we found no differences in the baseline characteristics between this expanded case sample and the complete case sample, both the K/L grade and knee injury were predictors of all pain patterns, with the strongest association being with persistent pain.

Furthermore, the proportions of subjects in each pain group were similar. We only used quinquennial knee pain assessments within a 12-year period. Whether the pattern of knee symptoms at this level of infrequent review mirrors patterns with more frequent symptom assessment over a more comprehensive time span is unknown and requires further study. Given the sample studied, the results can be generalized only to female subjects in the community between the ages of 45 years and 80 years, and we only assessed knee pain and not other symptoms of knee OA, such as stiffness and limited function. Unfortunately, we did not have the date of onset of pain recorded; this may raise methodologic issues, including recall bias and the definition of onset of knee pain, and we suggest that in future studies, such data be recorded.

Finally, we classified women as having incident knee pain if they experienced their first episode of pain at the final visit, even though it is not known if the pain would have persisted at later visits. We accept that this may have led to a degree of misclassification, which we hope to address as the cohort completes further followup visits.

Studying the long-term time course of pain has confirmed the presence of different patterns of pain, with a significant proportion of subjects demonstrating intermittent symptoms. This should be taken into ac-
count when either planning treatment strategies or using pain as an outcome or exposure variable in research studies, as a large minority of patients presenting with knee pain did not report pain at any of the subsequent quinquennial assessments.

The method used in this study gives rise to a novel approach for phenotyping patients with knee pain. We understand that validation of our findings by replication in other cohorts is required (23), ideally utilizing measures of knee symptoms at more frequent time intervals. However, the differential association of BMI and K/L grade with the pain pattern suggests that identifying pain phenotypes based on temporal patterns is likely to inform etiopathology.

In summary, we have identified significant variability in the time course of pain symptoms over a period of 12 years in this community-based prospective study of self-reported knee pain, with 9%, 24%, and 29% of subjects reporting persistent pain, incident pain, and intermittent pain, respectively. These subtypes of pain are associated with distinct baseline predictors, in which persistent pain over time was associated with the baseline BMI, K/L grade, and previous knee injury, whereas incident pain was associated with only BMI, and intermittent pain was associated with only previous knee injury. These findings need to be validated through reproduction in other cohorts and then applied in order to further our understanding of predictors of knee pain, thereby enhancing prevention and treatment strategies.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Arden had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Soni, Cooper, Spector, Arden.
Acquisition of data. Soni, Hart, Goulston, Spector, Arden.
Analysis and interpretation of data. Soni, Kiran, Leyland, Cooper, Javaid, Arden.

REFERENCES


