

# Does knee pain in the community behave like a regional pain syndrome? Prospective cohort study of incidence and persistence

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*Ann Rheum Dis* 2007;**66**:1190–1194. doi: 10.1136/ard.2006.061481

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Accepted 30 October 2006  
Published Online First  
17 November 2006

Knee pain is a common symptom in the general population.<sup>1</sup> In the UK, a community survey in Staffordshire found that 47% of people aged >50 years had experienced knee pain over a 12-month period, including 25% whose symptoms had lasted >3 months;<sup>2</sup> a second survey, in Nottingham, estimated the overall 12-month prevalence in 40–79 year olds at 29%, with rates tending to increase with age;<sup>3</sup> and a third, in Oxfordshire, estimated a 1-year prevalence of 33% in >65 year olds, among whom 58% were still in pain a year later.<sup>4</sup> In another survey from Staffordshire, 10% of knee pain sufferers had consulted their family doctor for over a year,<sup>5</sup> and in a study from Dutch primary care, most consulters remained symptomatic when followed up over 12 months.<sup>6</sup>

Knee pain can be caused by a variety of pathologies, including osteoarthritis (OA), tears of the meniscal cartilage, and tears and strains of the knee ligaments. Most knee pain in the community does not arise from OA and does not necessarily share the same risk factors.<sup>7–9</sup> In the NHANES-I study, only 15% of subjects with knee pain had radiologically established knee OA, while more than half of those with radiological OA were not in pain.<sup>10</sup> Furthermore, correlates of radiological disease (eg, sex, race, obesity) were generally not associated with knee pain, which showed a much stronger relation with poor psychological well-being.<sup>11</sup> Similarly, in several surveys of knee pain patients, mental ill-health was more evident in the absence of OA, and physical mechanical factors less so.<sup>12–14</sup> Hadler observed that: "the epidemiology of [knee] OA and the epidemiology of knee pain have little in common".<sup>7</sup>

Some authors have described knee pain in the community as a form of regional pain syndrome, similar to low-back pain (LBP), non-specific upper limb pain, or fibromyalgia.<sup>15 16</sup> If so, then in addition to mental ill-health,<sup>3 17</sup> it might share other risk factors in common with these complaints, such as health anxiety, poor self-rated health (SRH) and negative illness

**Objectives:** To investigate whether knee pain in the community behaves like a regional pain syndrome, determined by its association with mental health, self-rated health (SRH) and beliefs about prognosis.

**Methods:** An 18-month postal follow-up was conducted in 1798 working-aged subjects, sampled from the community. At baseline questions were asked about pain in the knee lasting  $\geq 1$  day in the previous 12 months, mental health (Short-Form 36), somatising tendency (elements of the Brief Symptom Inventory), SRH and concern about 12-month prognosis. At follow-up we asked about knee pain during the last 4 weeks, and whether it had been present for  $\geq 14$  days or prescription-treated. Associations with incidence and persistence were explored using logistic regression.

**Results:** The 1256 participants (70% response) comprised 468 with knee pain at baseline and 788 without. Among the former, 49% had persistent knee pain at follow-up, while among the latter, 15% reported new symptoms. Incident prescription-treated knee pain was strongly associated with all of the mental health variables and with SRH. The odds of knee pain persisting were significantly raised in the least versus most favourable bands of somatising tendency and SRH, and persistence was also significantly more common among those who at baseline were concerned that they would still have a problem in 12 months.

**Conclusions:** Our observations support the hypothesis that knee pain in the community shares risk factors in common with other non-specific regional pain syndromes.

beliefs. The evidence base on this is much more limited than for pain at other anatomical sites, and is largely cross-sectional in nature. It thus fails to distinguish cause from effect, and risk factors for incidence from those for persistence. Moreover, some potential risk factors such as general tendency to express distress from somatic symptoms (somatising tendency) do not seem to have been explored at all; and others that have proved important for the management of LBP have received only scant attention.<sup>6</sup>

As part of a population-based prospective study,<sup>18 19</sup> we therefore investigated whether somatising tendency, low mood, and poor SRH predict incidence and persistence of knee pain, and whether concern about prognosis predicts persistence.

## METHODS

The study sample was drawn from an earlier cross-sectional survey.<sup>18</sup> At baseline, a questionnaire had been mailed to a stratified random sample of 4998 subjects aged 25–64 years, chosen from the age–sex registers of five general practices in the west of England. Among a total of 2632 respondents, 1798 agreed to be followed up and were mailed a second time at an interval of 18 months, with a single reminder, if required, after a further 3 weeks. Ethical approval was provided by the NHS Southwest Local Research Ethics Committee.

## Baseline

At baseline, we asked about pain in the knee lasting  $\geq 1$  day during the past 12 months. Those who reported such pain provided supplementary details on the number of days or months of pain during this period, and about whether, at its worst, the pain made it difficult or impossible to sleep, dress or

**Abbreviations:** CI, confidence interval; LBP, low back pain; OA, osteoarthritis; OR, odds ratio; SRH, self-rated health

**Table 1** Characteristics of participants at baseline and follow-up

Characteristic at baseline	No. at baseline (n=1798) (%)	No. (%) at follow-up (n=1256) (%)
Sex:		
Male	816 (45)	562 (45)
Female	979 (54)	694 (55)
Unknown	3 (0.2)	
Age group (years):		
<35	236 (13)	131 (10)
35–39	189 (11)	114 (9)
40–44	241 (13)	165 (13)
45–49	268 (15)	188 (15)
50–54	266 (15)	200 (16)
55–59	354 (20)	274 (22)
≥60	244 (14)	184 (15)
Knee pain during past 12 months:		
Any	643 (36)	468 (37)
>6 months	149 (8)	107 (9)
Disabling	88 (5)	61 (5)
Self-rated health:		
Fair/poor	247 (14)	148 (12)
Somatisation score:		
Worst band	685 (38)	461 (37)
SF-36 MH score:		
Worst band	617 (34)	406 (32)
Combined mental health score:		
Worst band	345 (19)	216 (17)

do household tasks. Subsequently those with knee pain at baseline were subcategorised according to whether symptoms were “frequent” (present for ≥6 months in aggregate over the past year) or “disabling” (interfering with all three of sleeping, dressing and performing household tasks). Similar information was collected for LBP.

The initial questionnaire also included items on mental health, SRH and (in those with symptoms) concern about prognosis. Specifically, we assessed low mood using the mental health subscale of the Short-Form 36 (SF-36 MH),<sup>20</sup> tendency to somatise using elements of the Brief Symptom Inventory,<sup>21</sup> and SRH using the question “In general would you say your health is ... excellent/very good/good/fair/poor?”.<sup>22</sup> For low mood and somatising tendency, subjects were categorised into three bands representing thirds of the distribution of scores for all subjects. In addition, as described more fully elsewhere,<sup>19</sup> we created a composite mental health variable (composite mental health score) in three bands, based on the joint distribution of SF-36 MH and somatising tendency bands (worst = top third of both scales; best = bottom third of both scales; intermediate = other combinations). These questionnaire items have been assessed previously in various settings<sup>23–25</sup> and found by us to have predictive validity for regional pain at other sites.<sup>19</sup>

Finally, at baseline, we asked about occupation and whether a typical working day involved lifting weights ≥25 kg by hand, kneeling or squatting for >1 h, climbing a ladder, or digging and shovelling.

### Follow-up

The second questionnaire asked about knee pain lasting ≥1 day during the last 4 weeks of follow-up, including: (a) “any” knee pain; (b) “frequent” knee pain (ie, present for ≥14 days during the past 4 weeks); and (c) “prescription-treated” knee pain (knee pain for which prescription treatment had been taken during the past 4 weeks). All three outcomes were considered in analyses of persistence and incidence.

Subjects who were free of knee pain at baseline contributed to the analysis of risk factors for incidence, while those who

had symptoms at baseline were included in the analysis of persistence. Associations with baseline characteristics were assessed by logistic regression with adjustment for potential confounders, and findings were expressed as odds ratios (ORs), with associated 95% confidence intervals (CIs). All models were adjusted a priori for the general practice from which the subject was recruited and for age (in seven bands) and sex, both of which are potential risk factors for incidence and persistence.<sup>2 6 17 26 27</sup> Additionally, in analyses of persistence, we explored the impact of adjusting also for frequency of knee pain and disability for everyday tasks at baseline. However, as these features could lie on the causal pathway between mental health/beliefs and persistence of symptoms we present our findings both with and without this adjustment.

Finally, we performed two sensitivity analyses to test the robustness of our findings. As some knee pain could have been referred from the lower back, we repeated the main analyses for the subset of respondents with no LBP in the past 12 months at baseline. In addition, among those in work, we explored the effect of adjusting for social class (manual versus non-manual) and occupational physical activities at baseline (lifting weights, kneeling/squatting, climbing and digging/shovelling, defined as above).

All analyses were conducted using STATA version 9.2.

### RESULTS

Table 1 provides details of the response.<sup>19</sup> Usable responses were returned by 1256 (70%) of the subjects who were sent a follow-up questionnaire. Respondents, although somewhat older than those mailed (mean age 49 vs. 48 years), differed little by sex, frequency and severity of pain at baseline, SRH or indices of mental health. The final sample comprised 468 subjects with knee pain in the 12 months before baseline and 788 who were free of this symptom.

Persistence was common in the former group: 49% (95% CI 44%–53%) reported knee pain at follow-up, including 22% with frequent and 21% with prescription-treated knee pain (table 2). Incident symptoms were less common—15% for any knee pain and <5% for frequent and prescription-treated knee pain.

Table 3 shows the relation of incident knee pain to SRH and mental health at baseline. The odds of “any” knee pain and “frequent” knee pain were raised 1.4–1.8-fold in those in the worst band compared with the best band of each variable. Individual risk estimates were generally not significant at the 5% level, although in each case an exposure–response gradient was suggested. Associations with incident prescription-treated pain were stronger, although based on smaller numbers and with wider confidence intervals, and p values for trend were all statistically significant at the 1% level. Thus, for SF-36 MH (worst versus best band) the OR was 4.2 (95% CI 1.6 to 11.3), and it was similarly elevated for somatising tendency (OR 3.1,

**Table 2** Prevalence of knee pain in the last 4 weeks of follow-up according to pain status at baseline

Knee pain at baseline*	Knee pain in last 4 weeks of follow-up		
	Any n % (95% CI)	Frequent n % (95% CI)	Prescription treated n % (95% CI)
Knee pain absent (n=788)	119 (12.7 to 17.8) 15.1	30 (2.6 to 5.4) 3.8	34 (3.0 to 6.0) 4.3
Knee pain present (n=468)	227 (43.9 to 53.1) 48.5	102 (18.1 to 25.8) 21.8	96 (16.9 to 24.5) 20.5

\*Pain in the knee in the previous 12 months.

**Table 3** Associations of new onset knee pain with SRH and mental health at baseline

Characteristic at baseline	No. in sample*	Knee pain in last 4 weeks at follow-up			
		Any knee pain		Prescription-treated knee pain	
		No. with pain	OR (95% CI)	No. with pain	OR (95% CI)
<b>SRH</b>					
Excellent	125	17	1.0	None	
Good/very good	586	86	1.1 (0.6 to 1.9)	24	1.0†
Fair/poor	75	16	1.6 (0.7 to 3.4)	10	2.7 (1.2 to 6.2)
<b>Somatising tendency score</b>					
Best	285	35	1.0	7	1.0
Intermediate	240	34	1.1 (0.7 to 1.8)	6	1.0 (0.3 to 3.2)
Worst	239	46	1.6 (1.0 to 2.7)	18	3.1 (1.2 to 8.0)
<b>SF-36 MH score</b>					
Best	323	42	1.0	6	1.0
Intermediate	213	34	1.3 (0.8 to 2.2)	8	1.9 (0.6 to 5.7)
Worst	244	40	1.4 (0.9 to 2.3)	18	4.2 (1.6 to 11.3)
<b>Combined mental health score</b>					
Best	172	21	1.0	3	1.0
Intermediate	477	70	1.2 (0.7 to 2.1)	16	1.8 (0.5 to 6.5)
Worst	117	24	1.8 (0.9 to 3.4)	12	5.2 (1.4 to 20.1)

Separate models were constructed for each row variable. All risk estimates were adjusted for age (in seven bands), sex and practice. SRH, Self-rated health.

\*A few respondents failed to answer all the questions.

†As no subjects with prescription-treated knee pain reported "excellent" SRH, the baseline for comparison was redefined as "good/very good" SRH.

95% CI 1.2 to 8.0) and for combined mental health score (OR 5.2, 95% CI 1.4 to 20.1).

Table 4 summarises the equivalent findings for persistence of knee pain. Only a weak association was found with SF-36 MH, but associations with the other variables were stronger, and all worst versus best band comparisons were significant at the 5% level with positive exposure–response relationships. ORs ranged from 2.4 to 14.4, being especially strong for SRH (frequent and prescription-treated knee pain) and combined mental health score ("any" and prescription-treated knee pain). Adjustment for frequency of knee pain and the presence of associated disability at baseline (Model 2) only weakened associations slightly.

Table 5 shows relations between persistence of knee pain and concern about prognosis. After adjustment for age, sex and practice, the odds of persistent pain were increased about threefold in subjects who were concerned that their knee pain would still be a problem in 12 months time (Model 1). ORs were little changed after additional adjustment for frequency of knee pain and report of disability at baseline (Model 2), and for Model 2 factors plus combined mental health score (Model 3).

Finally, in two sets of sensitivity analyses we explored the effects of excluding subjects with LBP at baseline and of adjusting for occupational physical activities. The former analyses were based on 354 subjects without and 156 with knee pain at baseline. Associations with SRH and indices of mental health were, if anything, strengthened in this analysis. Thus, for example, the OR for somatising tendency (worst

versus best band) was 2.7 (95% CI 1.2 to 6.0) for incidence of "any" knee pain and 5.3 (95% CI 1.8 to 15.4) for persistence of "any" knee pain, as compared with ORs of 1.6 and 3.6, respectively, for the whole sample. Our occupational analysis was based on 613 workers without knee pain and 328 workers with knee pain at baseline. Several of the physical risk factors we inquired about showed univariate associations with knee pain incidence (especially kneeling or squatting >1 h/day and being a manual worker) or knee pain persistence (especially climbing a ladder); however, associations with SRH and the mental health variables were only slightly lower when social class and all of the physical occupational risk factors were added to the main regression models and the analyses for tables 3–5 repeated (data available on request).

## DISCUSSION

Our findings indicate that incidence and persistence of knee pain in working age adults from the general community are both significantly associated with low mood, tendency to somatise, and poor SRH, and that concern over prognosis is a determinant of persistence. Associations tended to be stronger for more severe outcomes, and to exhibit exposure–response relations. Somatising tendency was a stronger predictor of persistence than low mood. Although physical activities at work were moderate independent risk factors for incidence and persistence, they did not confound or explain the associations with mental health or health beliefs.

Knee pain is likely to follow a relapsing and recurring course for many individuals, and this poses challenges in the definition of incidence and persistence. For each outcome we looked for symptoms during the final 4 weeks of follow-up. For incidence, we also required subjects to be free of symptoms for the 12 months prior to baseline (rather than the past 4 weeks, as in some other studies), to distinguish new episodes from ongoing symptoms. Persistence was defined in terms of symptoms at baseline and follow-up; it should be recognised, however, that some subjects may have enjoyed symptom-free periods in between.

Our findings need to be judged in the context of several strengths and weaknesses of study design. The original sampling frame (patients registered with British general practices) is likely to have been representative of the general population in the area studied (almost everyone in Britain registers with a family doctor). The sample size was fairly large, and the follow-up rate was reasonable at 70%. Furthermore, responders and drop-outs were similar in terms of the main study factors of interest. Although the final study sample represented only a minority of those canvassed at the initial cross-sectional phase, we have no reason to expect responders to be unrepresentative of the population at large in terms of longitudinal associations between mental health and knee pain. It also seems unlikely that selective response at baseline and at follow-up could bias findings so as to create artefactually the multiple exposure–response relationships observed. Also, to the extent that the survey was presented to participants as a general study of aches and pains in the community, in which knee pain was not a particular focus, they are likely to have blinded to the main hypotheses tested here.

One weakness was that respondents with knee pain were not subject to radiological investigation or detailed clinical assessment. A second was that no space could be allotted, in a broad questionnaire about multisite regional pain, to certain risk factors (body mass index and past history of knee injury) that ideally would have been controlled for in analysis. The former is a clear limitation, but we believe the impact of the latter to be slight. The relation of knee pain to physical mechanical factors seems less strong in those without OA (probably the majority of

**Table 4** Associations of persistence of knee pain with self-rated health and mental health at baseline

Characteristic at baseline	Knee pain in last 4 weeks at follow-up		
	No with pain/No in sample	Model 1 OR (95% CI)	Model 2 OR (95% CI)
<b>"Any" knee pain</b>			
Self-rated health			
Excellent	17/45	1.0	1.0
Good/very good	157/348	1.2 (0.6 to 2.3)	1.2 (0.6 to 2.3)
Fair/poor	52/73	3.4 (1.5 to 7.7)	2.8 (1.2 to 6.7)
Somatising tendency score			
Best	25/90	1.0	1.0
Intermediate	61/140	1.9 (1.1 to 3.5)	1.7 (0.9 to 3.2)
Worst	131/222	3.6 (2.1 to 6.3)	3.2 (1.8 to 5.7)
SF-36 MH score			
Best	77/168	1.0	1.0
Intermediate	60/133	1.0 (0.6 to 1.6)	1.0 (0.6 to 1.6)
Worst	86/162	1.4 (0.9 to 2.1)	1.3 (0.8 to 2.1)
Combined mental health score			
Best	11/48	1.0	1.0
Intermediate	151/306	3.5 (1.7 to 7.3)	2.8 (1.3 to 6.0)
Worst	55/99	4.3 (1.9 to 9.7)	3.4 (1.5 to 7.8)
<b>Frequent knee pain</b>			
Self-rated health			
Excellent	3/45	1.0	1.0
Good/very good	68/348	2.9 (0.8 to 9.7)	2.7 (0.7 to 9.7)
Fair/poor	31/73	7.8 (2.1 to 28.7)	5.8 (1.4 to 23.5)
Somatising tendency score			
Best	10/90	1.0	1.0
Intermediate	28/140	1.8 (0.8 to 3.9)	1.5 (0.6 to 3.6)
Worst	61/222	2.8 (1.3 to 5.8)	2.3 (1.1 to 5.3)
SF-36 MH score			
Best	36/168	1.0	1.0
Intermediate	25/133	0.9 (0.5 to 1.6)	0.8 (0.4 to 1.5)
Worst	41/162	1.2 (0.7 to 2.1)	1.1 (0.6 to 2.1)
Combined mental health score			
Best	6/48	1.0	1.0
Intermediate	66/306	1.8 (0.7 to 4.5)	1.1 (0.4 to 3.1)
Worst	27/99	2.4 (0.9 to 6.6)	1.5 (0.5 to 4.5)
<b>Prescription-treated knee pain</b>			
Self-rated health			
Excellent	2/45	1.0	1.0
Good/very good	58/348	3.5 (0.8 to 15.4)	3.5 (0.7 to 16.2)
Fair/poor	36/73	14.4 (3.1 to 67.1)	12.1 (2.4 to 60.9)
Somatising tendency score			
Best	8/90	1.0	1.0
Intermediate	18/140	1.3 (0.5 to 3.2)	1.1 (0.4 to 2.9)
Worst	65/222	3.4 (1.5 to 7.7)	2.9 (1.2 to 6.9)
SF-36 MH score			
Best	26/168	1.0	1.0
Intermediate	29/133	1.5 (0.8 to 2.8)	1.5 (0.8 to 3.0)
Worst	39/162	1.5 (0.8 to 2.7)	1.4 (0.7 to 2.6)
Combined mental health score			
Best	3/48	1.0	1.0
Intermediate	59/306	3.4 (1.0 to 11.9)	2.7 (0.8 to 9.9)
Worst	29/99	5.5 (1.5 to 20.0)	4.0 (1.0 to 15.5)

Separate models were constructed for each row variable. In Model 1 risk estimates were adjusted for age, sex and general practice. In Model 2, risk estimates were adjusted for age, sex, general practice and characteristics of pain at baseline (frequency and associated disability).

our study sample); confounding could only explain associations with psychological risk factors if uncontrolled variables were common and important risk factors for knee pain, and were unequally distributed between exposure groups according to the dose-response gradients we found. This seems unlikely.

A more plausible explanation of the findings is that most cases of knee pain in the community behave like LBP and non-specific upper limb pain, in sharing the characteristics and associations of regional pain syndromes. Thus persistence of LBP has been associated with poor SRH,<sup>28, 29</sup> fear-avoidance

**Table 5** Associations of persistent knee pain with concern over prognosis

	Knee pain in last 4 weeks of follow-up		
	Any	Frequent	Prescription-treated
Concerned knee pain will still be a problem in 12 months (n, %):			
No	24/95 (25%)	6/95 (6%)	5/95 (5%)
Yes	202/367 (55%)	96/367 (26%)	91/367 (25%)
OR (95% CI)			
Model 1	3.3 (2.0 to 5.5)	4.6 (1.9 to 11.0)	5.4 (2.1 to 14.1)
Model 2	2.7 (1.6 to 4.6)	2.6 (1.1 to 6.5)	3.8 (1.4 to 10.2)
Model 3	2.7 (1.5 to 4.8)	3.2 (1.2 to 8.7)	6.2 (1.8 to 21.2)

In Model 1 risk estimates were adjusted for age, sex and practice. In Model 2 risk estimates were adjusted for age, sex, practice, and characteristics of pain at baseline (frequency and associated disability). In Model 3 risk estimates were adjusted for age, sex, practice, characteristics of pain at baseline (frequency and associated disability), and combined mental health score.

beliefs,<sup>30</sup> pessimism over prognosis,<sup>31, 32</sup> depression,<sup>28</sup> and somatising tendency,<sup>28</sup> while incident LBP pain has been linked with poor SRH<sup>33</sup> and poor SF-36 MH,<sup>34</sup> our data imply that similar basic relationships hold for incidence and persistence of pain at the knee.

Direct support for this inference from other sources is limited. In contrast to LBP, there have been few studies of incident knee pain in the community,<sup>16, 35</sup> and none of the persistence of knee pain as such, although there have been a few investigations of persistent pain in established cases of OA from the community.<sup>13, 16, 17</sup> Few knee pain studies have explored mental health and belief variables as potential risk factors. Indeed, we believe this to be the first community-based cohort study of mental health factors, self-rated health, beliefs and incident knee pain. The findings on somatising tendency as a predictor of incidence and persistence also appear to be novel. However, two studies have reported that self-efficacy beliefs (negative self-beliefs about performance capability) are longitudinal predictors of decline in function,<sup>17, 35</sup> and one follow-up study of established knee OA suggested that poor SF-36 MH predicts a poor functional outcome at 18 months.<sup>17</sup> A recent study among knee pain consulters from Dutch primary care found also that somatic distress (assessed by the short version of the Four Dimension Symptom Questionnaire) was a significant predictor of less favourable changes in pain intensity at 3 and 12 months, and less favourable function at 12 months.<sup>6</sup>

Our findings also agree with several cross-sectional studies involving community samples. Thus, in a postal survey of 4057 adults from Nottingham, the odds of knee pain were doubled, and those of disabling knee pain raised 4.7-fold in subjects with poor SF-36 MH;<sup>3</sup> in a cohort of newly employed workers, the odds of knee pain in the past month were doubled in those with psychological distress (General Health Questionnaire score  $\geq 3$  vs. 0);<sup>36</sup> in the cross-sectional phase of the current study, we reported strong associations between somatising tendency and disabling or chronic knee pain;<sup>18</sup> and among 374 subjects from a study of ageing in Baltimore, anxiety scores were associated with a lifetime history of knee pain, with differences confined to those with normal radiological findings.<sup>10</sup> However, cross-sectional studies reveal little about cause and effect. Thus, Hannan *et al* found it "unclear whether anxiety is a risk factor

for pain reporting, or whether ... subjects were more anxious because they had pain";<sup>10</sup> and similarly, at baseline, we raised a question as to whether subjects with a low threshold for being bothered by somatic symptoms more readily reported distressing regional pain, or whether the experience of chronic pain heightened bodily awareness of physiological events.<sup>18</sup> In studies of persistence, even a prospective design may not circumvent the pitfall of reverse causation, as more severe symptoms at baseline may cause psychological distress and at the same time carry a worse prognosis. The most persuasive evidence on causal relations comes from cohort studies of incidence.

Our report adds to the sum of knowledge in providing incidence data and in confirming that mental health and health beliefs are factors in incident knee complaints as well as in the persistence of old knee complaints. Associations were particularly strong for knee pain that was medically treated—an effect that could reflect perceptions about severity, or illness behaviour, or both. Whichever the case, our findings support the hypothesis that knee pain in the community shares several risk factors in common with other non-specific regional pain syndromes.

## ACKNOWLEDGEMENTS

We are grateful to the five general practices from Avon that allowed us to approach their patients and assisted with the initial sampling; also to Gwen Coombs and the MRC staff in Southampton and Bristol who helped with co-ordinating the follow-up mailing; the staff who assisted with data processing and programming support; and the patients who participated in the study. Denise Gould prepared the manuscript.

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**Funding:** This project was supported by the MRC Health Services Research Collaboration, Department of Social Medicine, University of Bristol and by core funding from the Medical Research Council.

Competing interests: None

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