## Original article

# Inadequate pain relief and large functional loss among patients with knee osteoarthritis: evidence from a prospective multinational longitudinal study of osteoarthritis real-world therapies

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#### **Abstract**

**Objective.** To estimate the prevalence of inadequate pain relief (IPR) among patients with symptomatic knee OA prescribed analgesic therapy and to characterize patients with IPR.

**Methods.** Patients  $\geqslant$  50 years old with physician-diagnosed knee OA who had taken topical or oral pain medication for at least 14 days were recruited for this prospective non-interventional study in six European countries. Pain and function were assessed using the Brief Pain Inventory (BPI) and the WOMAC; quality of life (QoL) was assessed using the 12-item short form. IPR was defined as an average pain score of >4 out of 10 on BPI question 5.

**Results.** Of 1187 patients enrolled, 68% were female and the mean age was 68 years (s.p. 9); 639 (54%) met the definition of IPR. Patient responses for the BPI average pain question were well correlated with responses on the WOMAC pain subscale (Spearman r = 0.64, P < 0.001). In multivariate logistic regression, patients with IPR had greater odds of being female [adjusted odds ratio (adjOR) 1.90 (95% CI 1.46, 2.48)] and having OA in both knees [adjOR 1.48 (95% CI 1.15, 1.90)], higher BMI, longer OA duration, depression or diabetes. Patients with IPR (vs non-IPR) were more likely to have worse QoL, greater function loss and greater pain interference.

**Conclusion.** IPR is common among patients with knee OA requiring analgesics and is associated with large functional loss and impaired QoL. Patients at particular risk of IPR, as characterized in this study, may require greater attention towards their analgesic treatment options.

Trial registration: https://clinicaltrials.gov/ (NCT01294696).

Key words: analgesic therapy, inadequate pain relief, knee, osteoarthritis.

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#### Introduction

Since 1990 the prevalence of musculoskeletal disorders has increased 45% and these disorders represent the second largest cause of disability worldwide, accounting for 21% of global years lived in disability [1]. Of the musculoskeletal disorders, OA represents the most common form of joint disease [2, 3]. Risk factors including older age, female gender, obesity and a history of manual labour result in susceptibility of the joints to damage, repair failure and OA [3–5].

OA of the knees accounts for 83% of the total OA burden and ranks among the top 10 non-communicable diseases for global disability-adjusted life years (DALYs; i.e. years of life lost and years lived with disability) [1, 3]. Clinical outcomes for people with knee OA typically involve pain, limitations of daily living activities, physical disability and overall reduction of quality of life (QoL).

As there is no cure for OA, the goals of OA therapies are to reduce the levels of pain and inflammation, slow cartilage degradation, improve function and reduce disability. Evidence-based guidelines recommend a broad range of pharmacological and non-pharmacological therapies for OA pain management [6–13]. Commonly used therapies and treatment modalities include paracetamol, NSAIDs, opioids, topical analgesics and IA injection of corticosteroid [5–12]. It is not possible to predict which therapy will work for any individual patient, and response is not uniform across populations [9, 14].

In both OA clinical trials and clinical practice, outcome assessments have traditionally been limited to evaluation of pain intensity [15]. The focus of clinical trials for OA analgesic therapies has been on treatment response, while the consequences of inadequate response are less well investigated [16]. Moreover, the outcomes of clinical trials do not directly translate to the real world, where patients may experience greater pain, have multiple comorbidities and use their pain medications intermittently.

Thus an important issue facing people with OA and their health care providers is inadequate pain relief (IPR). As a concept, IPR has not been widely explored in OA, and there is limited understanding of the relationship between IPR and patient factors, treatment patterns and QoL. A better understanding of IPR—and of the characteristics of patients likely to experience IPR—may help clinicians to identify patients who require close monitoring and careful selection of therapy for OA.

The objectives of this multinational prospective observational study, the Study of Osteoarthritis Real World Therapies (SORT), were (i) to estimate the prevalence of IPR among patients with symptomatic knee OA prescribed analgesic therapy, (ii) to assess the characteristics of patients with IPR and (iii) to examine the relationship between IPR and health outcomes, comparing patients with IPR versus non-IPR in terms of history and clinical care at baseline.

### **Methods**

## Study design and patients

This prospective longitudinal cohort study was conducted at 53 centres in six European countries (the UK, France, Germany, Portugal, The Netherlands and Italy). Centres included both general and specialist practices, varying by country (see supplementary Table S1, available at *Rheumatology* Online). Patients were recruited from November 2011 to January 2012. This analysis presents baseline pain data, demographic data and medication use, as well as the associations with other health outcomes

at baseline. Clinical and demographic data for patients who declined to participate were not collected.

Patients eligible for study enrolment were ≥50 years old with a physician's diagnosis of OA of one or both knees [17] and were prescribed, at the direction of a physician, topical or oral pain medications for at least 14 days before entering the study. Patients were excluded if they had any arthritis other than primary OA, partial or total joint replacement in the affected knee(s) or treatment with DMARDs

As this was a real-world observational study, no medications or interventions were provided under the study protocol. Participation in the study did not influence the choice of treatment; patients' treatments were determined by their attending physicians. Patients could elect to withdraw at any time without impact on their medical care. The study protocol was approved by the local ethics committee at each site and each patient gave written informed consent according to the Declaration of Helsinki. The study was registered with ClinicalTrials.gov (NCT01294696).

#### Data collection

At study entry, demographic information, medical history and medication use were collected. Patients completed questionnaires regarding their knee OA, including assessments of pain level, joint stiffness, physical functioning, satisfaction with and response to treatment and QoL. All questionnaires were provided to patients in their local language.

Patients were instructed to assess pain caused by OA in the affected knee(s) using the Brief Pain Inventory (BPI). The BPI is a comprehensive instrument validated in several languages for assessing pain severity and pain interference with function [18–21]. Pain relief was derived using question 5 of the BPI, which assesses average pain: Please rate your pain by circling the one number that best describes your pain on the average. The numerical rating scale ranges from 0 (no pain) to 10 (pain as bad as you can imagine). This single question is similar to how physicians would evaluate their patients' pain in most clinical encounters and is of clear clinical relevance.

Other patient self-assessments were collected, including pain, stiffness and physical function in the knee as measured by the WOMAC questionnaire (0-100 mm visual analogue scale) [22] and QoL as assessed by the Medical Outcomes Trust 12-item Short Form Health Survey (SF-12) [23].

Patients also reported their satisfaction with symptomatic treatment for knee OA, as measured by two questions regarding pain relief and tolerability of medication over the previous 7 days. These questions were assessed on a five-item categorical scale ranging from very dissatisfied to very satisfied. Patients and investigators reported the response to therapy on a five-item scale from no response to excellent response using the Patient Global Assessment of Response to Therapy Questionnaire (PGART) and the Investigator Global Assessment of Response to Therapy Questionnaire (IGART) [24], respectively.

#### Study endpoint

The primary endpoint was the patient's assessment of pain relief at study entry. In clinical trials, assessments of pain caused by OA are based on cut-off points for patient-reported pain, function and global assessments [25]. Different pain cut-off points have been used previously to categorize pain severity [26] and manageable pain [27]. In a recent review of pain measures and associated cut-off points, it was reported that patients reported that  $\leqslant 3$  on a 10 point scale is thought to be no worse than mild pain [28]

Question 5 of the BPI, which assesses average pain, defines mild pain as a pain score of 0-4, moderate pain as 5-6 and severe pain as 7-10 [29]. In this study, IPR was defined as a score >4 (moderate or severe pain) on BPI question 5; scores of 0-4 were classified as non-IPR.

#### Statistical analyses

The primary analysis was a cross-sectional comparison of IPR vs non-IPR patient cohorts at baseline. Study endpoints, patient characteristics and treatments for knee OA were summarized using descriptive statistics. Categorical variables were compared using the  $\chi^2$  test or Fisher's exact test, while continuous variables were compared using the Mann–Whitney Wilcoxon test.

We examined the robustness of the cut-off point of 4 on the BPI in identifying the prevalence of IPR by comparing adjacent cut-off points found in the literature (pain  $\leq 3$  as no worse than mild pain and pain >5 [29]) and observed the distribution of patients classified as IPR. In addition, we reviewed the distribution of the BPI average score and its association with the WOMAC pain subscale using Spearman's rank-order correlation coefficient. We also compared the different IPR cut-off points using the WOMAC pain subscale, WOMAC physical function subscale and SF-12 Physical Component Summary scores. To accomplish this, following Tan *et al.* [30], we employed an analysis of variance (ANOVA) using IPR categories derived from the BPI average score as the independent variable and the other measures as dependent variables.

To identify the characteristics of patients who were more likely to have IPR, a multivariate logistic regression model was employed, adjusting for country effects. The following variables were assessed: age, female sex, BMI, years since OA diagnosis, clinical diagnosis of both knees, co-morbidities (cardiovascular disease, renal impairment/failure, diabetes, depression, hyperlipidaemia, hypertension) and a number of different classes of medication.

All analyses were conducted using SAS version 9.3 (SAS Institute, Cary, NC, USA). Statistical significance was set at P < 0.05.

#### **Results**

A total of 1187 consenting patients were enrolled in the study at 53 centres in six countries. Table 1 summarizes patient characteristics at baseline and Supplementary Table S2, available at *Rheumatology* Online, presents patient enrolment numbers by country. The mean patient age

was 68 years, 68% of patients were women and only 19% of patients were in paid employment at the time of study enrolment. The most common physician-reported co-morbidity was hypertension, affecting 58% of patients. Just over half of the patients (52%) had OA affecting both knees, while nearly one-quarter each had an affected left or right knee (Table 1).

#### Prevalence of IPR

At the baseline assessment, 639/1187 patients [54% (95% CI 51%, 57%)] reported IPR as measured on the BPI average pain score. The prevalence of IPR was quite robust to the definition using different cut-off points. With a cut-off point of  $\leqslant$ 3 defining patients with no worse than mild pain, the inverse number of patients was 846/1187 [71% (95% CI 69%, 74%)] meeting the definition for IPR (i.e. a BPI score > 3). A cut-off point > 5 classified 414 [35% (95% CI 32%, 38%)] patients as having IPR.

Patient responses for the BPI average pain question were well correlated with responses on the WOMAC pain subscale (Spearman's  $r\!=\!0.64$ ,  $P\!<\!0.001$ ,  $n\!=\!1109$ ), further demonstrating that the concept of IPR is not an artefact of how IPR is defined and assessed. Fig. 1 depicts the distribution of patients in the IPR and non-IPR cohorts according to WOMAC pain subscale scores, which were converted to a 0-10 point scale to facilitate comparison.

The cut-off point of 4 was optimal in our sample, with the highest *F* values in the ANOVAs when BPI pain severity, BPI pain interference and SF-12 Physical Component Summary scores were the dependent variables and near optimal when the WOMAC pain subscale and WOMAC physical function subscale were the dependent variables (see Supplementary Table S3, available at *Rheumatology* Online).

#### Characteristics of patients with IPR

While patients in both the IPR and non-IPR cohorts were of similar mean age (68 years) and included similar percentages of current smokers (8%), the two groups were significantly different for multiple characteristics, as outlined in Table 1. Patients reporting IPR were more likely to be female and less likely to be employed; they had a higher mean BMI and a longer mean duration of OA; and they had a greater likelihood of co-morbid hypertension, current or prior depression, diabetes and current or prior renal impairment or failure ( $P \le 0.027$  for all comparisons). In addition, a significantly greater percentage of patients with IPR had OA affecting both knees (P < 0.001) and physician-reported partial or total disability (P = 0.009; Table 1). While NSAIDs were the most commonly prescribed medication in both cohorts (65% overall), patients in the IPR cohort were significantly more likely (P < 0.001) to be prescribed paracetamol (44% vs 34% in non-IPR cohort) or opioid-containing medication (26% vs 16%).

After adjusting for country fixed effects, there were several significant predictors of IPR (Table 2). Specifically,

Table 1 Baseline demographic characteristics of all patients and by knee pain relief at baseline

	All patients ( <i>n</i> = 1187)	IPR (n = 639)	non-IPR ( <i>n</i> = 548)	P-value
Age, mean (s.d.), years	67.8 (9.4)	68.0 (9.8)	67.6 (9.0)	0.484
Female, n (%)	808 (68.1)	479 (75.0)	329 (60.0)	< 0.001
BMI, mean (s.p.), kg/m <sup>2</sup>	29.4 (5.5)	30.0 (5.7)	28.7 (5.1)	< 0.001
Number of classes of medication, mean (s.p.) <sup>a</sup>	1.5 (0.7)	1.5 (0.7)	1.4 (0.7)	0.008
Currently in paid employment, n (%) <sup>b</sup>	229 (19.4)	103 (16.3)	126 (23.1)	0.003
Current smoker, n (%)	95 (8.0)	49 (7.7)	46 (8.4)	0.431
Co-morbidity, n (%)				
Cardiovascular disease <sup>c</sup>	265 (22.3)	154 (24.1)	111 (20.3)	0.124
Hypertension	692 (58.3)	396 (62.0)	296 (54.0)	0.007
Hyperlipidaemia	533 (44.9)	297 (46.5)	236 (43.1)	0.242
Depression <sup>d</sup>	298 (25.1)	197 (30.8)	101 (18.4)	< 0.001
Diabetes	213 (17.9)	145 (22.7)	68 (12.4)	< 0.001
GI condition <sup>e</sup>	157 (13.2)	92 (14.4)	65 (11.9)	0.229
Renal impairment/failure <sup>d</sup>	80 (6.7)	53 (8.3)	27 (4.9)	0.027
Years since OA diagnosis, mean (s.d.)	6.2 (6.2)	6.9 (6.6)	5.4 (5.6)	< 0.001
Median (IQR)	4.5 (1.3, 9.6)	5.5 (1.5, 10.6)	3.7 (0.9, 8.4)	< 0.001
Clinical diagnosis of OA, n (%)				
Left knee only	286 (24.1)	146 (22.9)	140 (25.6)	0.307
Right knee only	282 (23.8)	120 (18.8)	162 (29.6)	< 0.001
Both knees	619 (52.2)	373 (58.4)	246 (44.9)	< 0.001
Hip	290 (24.4)	168 (26.3)	122 (22.3)	0.119
Spine	522 (44.0)	289 (45.2)	233 (42.5)	0.379
Physician-reported disability—partial or total, n (%)	154 (13.0)	98 (15.3)	56 (10.2)	0.009
Hip replacement—partial or total, $n$ (%)	70 (5.9)	45 (7.0)	25 (4.6)	0.083
Analgesic medication for OA, n (%)				
NSAID	773 (65.1)	389 (60.9)	384 (70.1)	< 0.001
Paracetamol	470 (39.6)	282 (44.1)	188 (34.3)	< 0.001
Alternative therapy <sup>f</sup>	211 (17.8)	104 (16.3)	107 (19.5)	0.149
Opioid-containing medication	254 (21.4)	169 (26.5)	85 (15.5)	< 0.001
Other	50 (4.2)	32 (5.0)	18 (3.3)	0.150

IPR was defined as an average Brief Pain Inventory pain score of moderate or greater pain (score >4) and non-IPR was defined as a score ≤4. <sup>a</sup>The classes of medication are NSAID, paracetamol, alternative therapy, opioid-containing medication and other. <sup>b</sup>Employment data were missing for eight patients—five in the IPR cohort and three in the non-IPR cohort. <sup>c</sup>Cardiovascular disease included congestive heart failure or established ischaemic heart disease, peripheral arterial disease or cerebrovascular disease. <sup>d</sup>Current or prior diagnosis. <sup>e</sup>GI conditions included IBD, active peptic ulceration or GI bleeding, perforation related to previous NSAID use, recurrent peptic ulcer or GI haemorrhage. <sup>f</sup>Alternative therapies included glucosamine, chondroitin and hyaluronate. GI: gastrointestinal; IQR: interquartile range; IPR: inadequate pain relief.

patients who reported IPR had greater odds of being female and having higher BMI, more years with OA diagnosis, a clinical diagnosis of OA in both knees, current or prior depression and a diagnosis of diabetes.

#### IPR and health outcomes

As shown in Table 3, patients in the IPR cohort had significantly greater overall pain severity and much worse pain interference on the BPI compared with patients in the non-IPR cohort (P < 0.001 for all comparisons). Similarly, the WOMAC subscale scores (pain, physical function and stiffness) were significantly worse (P < 0.001) for patients in the IPR cohort.

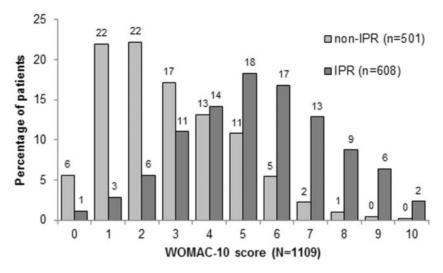
The Patient and Investigator Global Assessments of Response to Therapy showed significantly worse responses ( $P \le 0.004$ ) to immediate prior therapy for patients in the IPR cohort versus the non-IPR cohort (Table 3). In addition,

responses for all QoL domains on the SF-12 were significantly worse for those with IPR (Table 4). Overall, 51% of patients in the IPR cohort reported their general health status to be fair or poor as compared with 31% of the non-IPR cohort (P < 0.001). At baseline, 48% of patients with IPR reported dissatisfaction with response to treatment and 38% reported dissatisfaction with tolerability of medication.

#### **Discussion**

The results of this observational study indicate that IPR is a highly prevalent problem among patients with OA. After  $\geqslant 2$  weeks of physician-prescribed treatment, more than half of patients with knee OA reported IPR, as defined by moderate to severe pain (score >4) using the BPI average pain question. The prevalence of IPR could be as high as 70% if a pain score  $\leqslant 3$  (no worse than mild pain [29]) was used as the appropriate treatment target. As

Fig. 1 Score distribution for the WOMAC pain subscale score (converted to a 0–10 scale) by score on BPI question 5 as IPR (score >4) and non-IPR (score ≤4)



Percentages are patients in each cohort (IPR and non-IPR); 78 patients were missing WOMAC pain subscale data. IPR: inadequate pain relief; BPI: Brief Pain Inventory.

Table 2 Multivariable analyses examining the odds of IPR, adjusted for country fixed effects (n = 1187)

	Adjusted OR	95% CI
Female	1.90	1.46, 2.48
BMI	1.03	1.01, 1.06
Years since OA diagnosis	1.04	1.02, 1.06
Clinical OA diagnosis of both knees	1.48	1.15, 1.90
Cardiovascular disease	1.18	0.86, 1.62
Renal impairment/failure	1.29	0.77, 2.20
Baseline diabetes diagnosis	2.09	1.47, 3.01
Baseline depression	1.89	1.41, 2.54
Baseline hyperlipidaemia	0.88	0.68, 1.14
Baseline hypertension	1.15	0.88, 1.51
Number of different classes of medication	1.04	0.86, 1.26

Overall significance of the model: likelihood ratio  $\chi^2$  = 143.69, df = 17, P < 0.001. OR: odds ratio.

demonstrated in this study, patient responses on the BPI were well correlated with responses on the WOMAC pain subscale. Moreover, patients in the IPR cohort reported significantly worse scores on pain severity, pain interference, WOMAC function subscale and QoL (SF-12 Physical Component Summary) than patients in the non-IPR cohort.

Patients with IPR were a largely identifiable population who were more likely to be female and have longer disease duration, bilateral knee OA, greater opioid use and a higher prevalence of certain co-morbidities (hypertension, depression and diabetes). Clinicians should recognize this constellation of characteristics as constituting special risk, since patients with IPR were significantly more likely to be

unemployed and to be considered partially or totally disabled by their physician (15% vs 10% of those in the non-IPR cohort).

The fact that 54% of patients in this real-world setting had persistent moderate to severe pain suggests that currently prescribed pain treatments for knee OA are not meeting the needs of the majority of patients. The most commonly prescribed analgesic medications reported by patients were NSAIDs, followed by paracetamol and opioid-containing medications. These findings are consistent with those of prior observational studies indicating that management of OA in primary care may not conform to the recommendations in clinical practice guidelines or to the intensity of patients' pain [31–36].

For patients with knee OA, the importance of pain relief and functional improvement was evident in the results of a recently reported discrete choice experiment that assessed patient preferences with regard to NSAID-related benefits [36]. The patients with self-reported OA in that study ranked reduction in ambulatory pain and reduced difficulties associated with daily activities as the most important benefits.

The clinical characteristics of our patient population reflect those reported for the general population with OA with regard to age, sex and co-morbidities [4], suggesting that study patients are representative of patients with knee OA and that our findings are generalizable. Patient and investigator assessments of response to therapy were generally in agreement. Study results across the multiple and varied assessments of pain and functional outcomes were consistent, reinforcing the robustness of the findings as well as illustrating the marked differences between patients with IPR and non-IPR. It is noteworthy that patient assessments of pain relief were associated with other patient-reported assessments of function and

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TABLE 3 IPR and health outcomes by pain relief status

	IPR (n)	IPR (n = 639)	Non-IPR (n)	Non-IPR ( <i>n</i> = 548)	<i>P</i> -value
BPI, severity, <sup>a</sup> mean (s.p.)	637	5.8 (1.4)	547	2.7 (1.3)	<0.001
BPI, interference, a mean (s.p.)	636	5.3 (2.0)	548	2.5 (1.8)	< 0.001
WOMAC pain subscale, mean (s.d.)	608	53.6 (21.5)	501	28.5 (18.4)	< 0.001
Median (IQR)	608	53.2 (39.1-68.8)	501	25 (13.6-40)	
WOMAC stiffness subscale, mean (s.d.)	610	56.8 (26.3)	502	33.7 (25.3)	< 0.001
Median (IQR)	610	59.8 (41.5-77.5)	502	30 (12.5-50.5)	
WOMAC physical function subscale, mean (s.p.)	601	55.0 (21.1)	498	29.9 (19.4)	< 0.001
Median (IQR)	601	56 (41-70.9)	498	26.9 (14.3-42.0)	
PGART					
Excellent	629	24 (3.8)	540	53 (9.8)	< 0.001
Good	629	164 (26.1)	540	247 (45.7)	< 0.001
Fair	629	259 (41.2)	540	177 (32.8)	0.004
Poor	629	137 (21.8)	540	41 (7.6)	< 0.001
No response	629	45 (7.2)	540	22 (4.1)	0.031
IGART					
Excellent	637	13 (2.0)	546	44 (8.1)	< 0.001
Good	637	155 (24.3)	546	262 (48.0)	< 0.001
Fair	637	282 (44.3)	546	165 (30.2)	< 0.001
Poor	637	156 (24.5)	546	67 (12.3)	< 0.001
No response	637	31 (4.9)	546	8 (1.5)	0.001

Scoring on the BPI ranges from 0 (best) to 10 (worst); scoring on the WOMAC ranges from 0 (best) to 100 (worst). <sup>a</sup>The BPI severity score is the mean of responses to questions 3-6; the BPI interference score is the mean of responses to questions 9A-G. IPR: inadequate pain relief; BPI: Brief Pain Inventory; PGART: Patient Global Assessment of Response to Therapy; IGART: Investigator Global Assessment of Response to Therapy; IQR: interquartile range.

TABLE 4 Questionnaire results for QoL on the SF-12

	IPR (n)	IPR (n = 639)	Non-IPR (n)	Non-IPR ( <i>n</i> = 548)	<i>P</i> -value
General health status, n (%)					
Excellent/very good/ good	636	309 (48.6)	545	378 (69.4)	< 0.001
Poor/fair	636	327 (51.4)	545	167 (30.6)	< 0.001
Physical functioning scale	633	27.9 (26.9)	546	49.8 (28.1)	< 0.001
Role physical scale	638	39.2 (25.1)	545	59.3 (23.8)	< 0.001
Bodily pain scale	639	37.4 (24.7)	548	59.7 (23.3)	< 0.001
General health scale	636	41.1 (25.2)	545	52.1 (22.5)	< 0.001
Vitality scale	633	40.4 (25.5)	540	53.2 (23.5)	< 0.001
Social functioning scale	631	57.4 (29.3)	544	78.4 (23.8)	< 0.001
Role emotional scale	636	57.2 (28.8)	548	74.5 (23.0)	< 0.001
Mental health scale	633	56.0 (23.4)	541	70.3 (19.7)	< 0.001
Physical Component Summary	624	35.0 (8.0)	533	41.2 (8.2)	< 0.001
Mental Component Summary	624	45.6 (11.3)	533	51.8 (9.0)	< 0.001

QoL: quality of life; SF-12: 12-item Short Form Health Survey. Data are presented as mean (s.p.) unless otherwise specified. Scoring on the SF-12 subscales ranged from 0 (worst) to 100 (best). IPR: inadequate pain relief.

QoL. This finding suggests that assessing pain relief in the clinic is an efficient way of assessing the patient's overall health status.

A possible limitation of the study is that of selection bias, as not all invited patients consented to participate in the study, and we are not certain that non-participants were similar to patients. Evidence of selective non-participation (by patients  $\geqslant$ 80 years, of lower socio-economic group and currently employed) was seen in an earlier prospective study of knee pain and knee OA in the

general population, although the authors found no effect on the distribution of WOMAC scores [37]. Our analysis is cross-sectional, therefore the causal link between IPR and functional status cannot be fully characterized. The 12-month follow-up period of this study will enable us to document the clinical course of pain and pain management in patients with OA. From the longitudinal analysis we can demonstrate an association between pain intensity and variability to a range of other health benefits (e.g. QoL, functional status and productivity).

#### Conclusion

IPR is common among patients with knee OA requiring analgesics, affecting 54% of patients in this study, and is associated with large functional loss and impaired QoL. There appears to be a patient profile at particular risk of IPR. Practitioners should actively evaluate pain management and the effectiveness of treatment response. In discussions with patients, practitioners should ensure that patients are communicating their concerns about pain medication and have a thorough understanding of their analgesic treatment options.

#### Rheumatology key messages

- Inadequate pain relief is common among patients with knee OA requiring analgesics.
- Patients with inadequate pain relief have functional loss and reduced quality of life.
- Inadequate pain relief predictors include female sex, higher BMI, longer OA duration, bilateral knee OA, depression and diabetes.

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#### Supplementary data

Supplementary data are available at *Rheumatology* Online.

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