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The impact of osteoarthritis disease severity on treatment patterns and healthcare resource use: analysis of real-world data

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Abstract (250 words; maximum allowed 250)

Objective: To understand treatment patterns and healthcare resource utilisation (HCRU) related to osteoarthritis (OA) disease severity in patients in five European countries.

Methods: Data were drawn from the Adelphi OA Disease Specific Programme (2017-18). Physicians classified their patients as having mild, moderate or severe OA, and provided details on their current prescribed therapy and HCRU, including HCP consultations, diagnostics and testing, and hospitalisations. Comparisons between disease severity groups were made using analysis of variance and chi-squared tests.

Results: The study included 489 physicians (primary care physicians, rheumatologists, orthopaedic surgeons) reporting on 3,596 of their OA patients: 24% mild, 53% moderate, and 23% severe disease. Both physicians and patients reported decreasing satisfaction with treatment with greater disease severity, despite the number of classes of prescribed drugs and increased use of opioids, which were used in almost half of patients with severe OA. For patients whose treatment was not effective, physicians prescribed the same therapy options which were cycled in subsequent treatment lines, with multiple treatment regimens being commonly used. Patients with greater symptom severity also had more physician consultations, while the numbers of tests/imaging, predominantly X-ray, conducted to diagnose or monitor OA, increased significantly with disease severity. The type of HCP involvement in patient management also varied by OA severity.

Conclusions: Across five European countries, the use of both non-pharmacological and pharmacological treatments increases with greater disease severity. Those with more severe disease place a greater demand on health care resource, with HCP consultations, tests, and hospital visits increasing with severity.

Introduction

Osteoarthritis (OA) is a chronic degenerative joint disease associated with pain and impaired function. Globally, the prevalence of OA is rising, due to the ageing population and presence of risk factors such as sedentary lifestyle and obesity, which can be both a cause and a consequence of OA (1-3). The growing prevalence of OA represents an increasing socioeconomic issue leading to a significant burden on healthcare services (2, 3)(1-3): it is estimated that more than 240 million persons worldwide have symptomatic, activity-limiting OA and, across Europe alone, it is estimated that more than 40 million individuals are affected by OA (4-6).

Pain is the predominant symptom of OA, contributing to functional limitations, reduced quality of life and increased healthcare resource utilisation (HCRU) (7, 8). Patients with OA incur greater HCRU and treatment-related costs compared to those without OA with respect to inpatient, emergency room and outpatient settings, with significant variation by anatomical site of OA (9, 10). Medical imaging also represents an important element of HCRU in OA, although there is a general consensus that the use of imaging tests should be limited and is not essential for diagnosis of OA in patients with typical presentation (11). Routine imaging for OA monitoring is not recommended unless there is unexpected rapid progression of symptoms or clinical deterioration that may require surgical intervention (11).

Disease severity may therefore be the key factor for patients and healthcare providers to consider when choosing the most suitable therapy, and also when trying to manage HCRU and costs associated with treatment (12, 13). Disease severity assessment is based on various factors including patient-reported symptoms, such as pain, functional limitations, and impaired quality of life and work productivity, as well as an objective assessment of structural damage based on imaging. Clinicians are therefore likely to use a composite of these elements when rating OA severity in routine practice (8, 14).

Guidelines for OA management recommend holistic assessment with a multidisciplinary approach that includes non-pharmacological, pharmacological, and surgical interventions (14-18). Importantly, there have been growing concerns for a number of years on the potential toxicity (especially in the US) and lack of benefits for opioids, which have been a staple in OA treatment recommendations (15, 19-22).

The objective of the current study was therefore to identify the association between OA disease severity, treatment patterns and HCRU, in a recent real-world healthcare setting in five European countries, and to determine from real-world evidence if there have been any changes in treatments and HCRU, consistent with guideline recommendations.

Methods

Data were derived from the Adelphi OA Disease Specific Programme™ (DSP), a non-interventional, cross-sectional survey of physicians and their patients in five European countries (France, Germany, Italy, Spain and the UK), conducted between 2017–2018. The methodology has been widely used and described previously (23).

Physician and patient selection

Physicians were identified from publicly available lists of healthcare professionals (HCPs) according to pre-defined selection criteria: practicing physicians were in one of three specialties (orthopaedics, rheumatology, or primary care) and made treatment decisions for at least 10 patients with diagnosed OA in a typical month. Candidate respondents were screened by telephone, and those who met the pre-defined eligibility criteria were invited to participate in the current study. Physicians completed patient record forms (PRF) for up to nine consecutive patients, based on information collated from their most recent consultation and from their OA-related medical history as recorded in electronic health records.

Data from patients with a confirmed diagnosis of peripheral joint OA and who were aged 18 years or older, were eligible for inclusion in the study. Data were excluded from the analysis if the patient had back and/or neck pain only. In addition, in view of the frequency of tendinitis-related shoulder pain, data were excluded if the patient had a diagnosis of shoulder OA that had not been confirmed by radiography (X-ray).

Outcomes

Physician-completed data derived from PRFs included patient demographics, clinical characteristics, number of affected joints, location of the most ‘troublesome’ joint, Charlson Comorbidity Index (CCI) (24), non-pharmacological therapy recommendations, over-the-counter (OTC) medication use and current and previous medication prescribed for OA. In addition, physicians recorded the utilisation of physician consultations, imaging for diagnosis and monitoring, non-pharmacological interventions, surgical interventions, and related inpatient and outpatient hospitalisations.

Physicians categorised patients as having mild, moderate or severe OA by assessing multifactorial characteristics of patients’ disease rather than pain symptoms only. These characteristics included severity of radiographic OA and joint space narrowing, frequency and severity of pain, number and severity of joints affected, impairment in function and ability to work, and efficacy of current medication regimen.

Pain severity and functional impairment were both measured on a 10-point scale, where 0 indicated no pain/no functional impairment and 10 indicated the worst pain imaginable/complete functional impairment. From this, mild, moderate, and severe pain/impairment was categorised (0-3; 4-6; 7-10, respectively). Similarly, satisfaction with current medication was measured on a 5-point Likert scale, ranging from 'very satisfied' to 'very dissatisfied'.

After providing informed consent, each patient with a physician-completed questionnaire was invited to fill out a self-completed questionnaire, which elicited details on non-pharmacological interventions they had used to manage their OA, and their overall satisfaction with their treatment.

Statistical analysis

In our study, continuous variables were described by frequencies, means and standard deviations (SD) and the different severity groups (mild, moderate, severe) compared using t-tests or analysis of variance (25). Categorical variables, described by frequencies and percentages, were compared using Mann-Whitney U test, Pearson's chi-square test or Fisher's exact test (25). All data were managed and analysed using SPSS v7.5 or Stata v16.1.

Ethical considerations

The study was conducted as a market research survey adhering to the ICC/ESOMAR International code on market and social research and the European Pharmaceutical Marketing Research Association (26) guidelines, and in full accordance with relevant legislation at the time of data collection (26, 27); ethics committee approval was therefore not required.

Results

Physician and patient population

A total of 489 physicians were drawn from three specialties, including 266 primary care physicians (PCPs), 101 rheumatologists and 122 orthopaedic surgeons who completed PRFs for 3,596 patients from France (n=672), Germany (n=743), Italy (n=671), Spain (n=747) and the UK (n=763). Of these, physicians reported 24.3% of patients (n=874) with mild, 52.9% of patients (n=1,904) with moderate and 22.7% of patients (n=818) with severe OA (Table 1). PCPs were responsible for treating over half of the patients (52.4%, n=1,885),

with 21.1% of patients (n=759) treated by rheumatologists, and 26.5% of patients (n=952) treated by orthopaedic surgeons, consistent with the severity of their disease.

Patient demographic and clinical characteristics

Over half of the patients were female (58.6%), 91.8% of patients were white/Caucasian, with a mean (SD) age of 66.4 (11.9) years (Table 1). Several differences were observed in patient demographics across physician-reported disease severity, for example, the mean body mass index (BMI) was higher with greater disease severity, and more patients were retired or unemployed with increasing severity of OA. The mean time since OA diagnosis increased across disease severity from 2.6 years in mild to 3.7 years in moderate to 4.5 years in severe OA (Table 2; all $p<0.05$).

The joints affected are presented in Table 2. Overall, patients had a mean (SD) of 2.6 (2.1) OA-affected peripheral joints, with a significantly higher number of joints affected with worsening disease severity (all $p<0.05$). Knee and hip OA were reported in 55.8% and 34.0% of all patients, respectively, and were the most common sites of OA in the study population (Table 2). Other frequently reported OA-affected joints included back (23.7%), hands and fingers (16.5%), shoulder (13.4%) and neck (10.9%). Physicians reported hypertension, diabetes, dyslipidaemia/high cholesterol, osteoporosis, anxiety, depression, and chronic lower back pain to be the most common comorbidities in the overall population.

Of those patients with previous surgery, almost one quarter of patients had received a hip replacement and approximately one half, knee replacement. The prevalence of the individual comorbidities increased with greater disease severity (all $p<0.05$ relative to mild). In addition, higher CCI scores and an increase in current pain and functional impairment were associated with greater disease severity (Table 2).

Current treatment patterns

Approximately half (48.7%) of patients reported that they utilised non-pharmacological treatments to manage their OA. The most commonly used interventions were avoidance of painful activities (35.8%), massage (30.7%) and weight loss (29.3%). A greater proportion of severe OA patients generally reported to be using non-pharmacological interventions than those with mild or moderate disease (Figure 1). These patterns were generally consistent across all countries surveyed (Supplementary Table S1), although almost one quarter of patients in Germany (22%) were seeing a psychotherapist or counsellor, and dietary supplements were used by over 10% of patients in Germany and Italy.

Most patients were currently prescribed medication for their OA, ranging from 65.0% of mild, 75.8% of moderate to 76.5% of severe OA patients. However, 17.8% of mild OA patients

had reportedly never been prescribed medication for their OA by any physician involved in their management compared with 12.4% and 7.9% of patients with moderate and severe OA, respectively. Non-pharmacological treatments were used in combination with pharmacological treatment by 37.4% of patients and this increased with greater disease severity (28.4% of mild, 29.9% of moderate and 41.2% of severe OA patients). Pharmacological treatment was prescribed without discussion around non-pharmacological interventions in 31.0% of patients. A small number of patients (16.0%) were also using OTC medication in addition to their non-pharmacological and pharmacological treatments.

Current medication use by class and disease severity showed that paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) (oral 79.7%, topical 20.3%) were more frequently prescribed than opioids (Figure 2A). Moderate and severe OA patients were prescribed a greater number of medications (mean 1.4 and 1.6 medications, respectively, both $p<0.05$ vs. mild). Current paracetamol use was greater in moderate (44.5%) and severe (48.9%) patients compared to mild patients (34.3%; both $p<0.05$), while the use of NSAIDs was inversely proportional to disease severity (mild 45.4%, moderate 42.7%, severe 37.9%). This differs from data on previous medication history which showed that significantly more severe patients had previously used NSAIDs than mild/moderate patients (Figure 2B). Intra-articular corticosteroids were used in relatively few patients overall, but current use increased with greater severity of OA (mild 2.9%, moderate 9.2%, severe 12.9%).

The proportion of treated patients using opioids (strong and weak combined) was significantly higher in severe OA patients (64.1%) compared to mild (16.7%) and moderate (35.4%) patients (both $p<0.001$; Figure 2A). Weak opioids (e.g. tramadol) had greater use than strong opioids (14.4% of mild, 28.4% of moderate and 40.4% of severe OA patients), with severe OA patients using strong opioids (e.g. morphine) more frequently (23.7%) than mild or moderate patients (2.3% of mild and 7.0% of moderate OA patients). Overall, treatment history showed that over half of patients with severe OA had used paracetamol and NSAIDs but noticeably fewer currently, while the use of opioids in the current severe cohort (Figure 2B) remained consistently high (59%).

Treatment patterns were generally consistent across all European countries with the most frequently prescribed medication being an NSAID, ranging from 49% of patients in France to 86% in Germany (Supplementary Table S2). Opioids were also commonly prescribed, ranging from 25% of patients in Germany to 51% in the UK.

Treatment regimen changes

Our data showed that patients had often tried several different regimens of pharmacological treatments for their OA (Table 3), with patients prescribed significantly more treatment combinations (predominantly paracetamol combined with NSAIDs and/or opioids) with greater disease severity (all $p<0.05$). However, for patients whose treatment was not effective, physicians prescribed the same few therapy options which were cycled in subsequent treatment lines, including traditional NSAIDs, non-opioid or other non-NSAID analgesics, weak opioids, cyclooxygenase-2 (COX-2) inhibitors, glycosaminoglycans and corticosteroids (Figure 3).

Most patients (59.7%) received monotherapy as their initial prescription drug regimen for their OA (59.7%), but this decreased significantly with disease severity (73.3% of mild, 59.7% of moderate and 46.4% of severe OA patients; all $p<0.05$), whereas the proportion receiving two or more prescribed medications increased with disease severity (Table 3). Those patients receiving more than one prescribed medication in their initial regimen were most likely to be prescribed a combination of paracetamol and an NSAID (13.6%), paracetamol and an opioid (5.7%), an NSAID and an opioid (4.4%), or a combination of all three (3.5%).

As patients switched regimens, the proportion of patients receiving monotherapy for their OA decreased and the prescription of two or more medications increased (59.6% at first regimen switch; 66.6% at second regimen switch). As the number of treatment switches increased, there was increased usage of opioids as part of a combination therapy with paracetamol and NSAIDs (5.5% of patients at first switch and 9.3% at the second switch, Table 3).

Physician and patient satisfaction with current medication

Almost one quarter of physicians (24.4%) reported dissatisfaction with their patients' current medication (Supplementary Figure S1), the most frequently reported reasons being inadequate response to medication (52.2%) and lack of improvement in the patient's quality of life (40.4%) both of which were reported more frequently with increased disease severity (all $p<0.05$), and a need for change in regimen, especially in mild patients (30.0%). Overall, physician dissatisfaction was reported for 42.2% of severe patients compared to 48.7% of moderate patients and 9.1% of mild patients. Similarly, less than half of patients (47%) were satisfied with their treatment, and reported decreasing satisfaction as severity increased (mild, 58%; moderate, 47%; severe, 32%).

Significant differences in physician-reported satisfaction were observed for patients by individual drug class (all $p<0.05$ across severity groups), with increasing severity associated

with decreased therapy satisfaction for patients receiving paracetamol (0.5% mild; 8.7% moderate; 32.3% severe), NSAIDs (1.5% mild; 5.8% moderate; 36.7% severe) and opioids (2.2% mild; 10.0% moderate; 30.6% severe).

Healthcare resource utilisation

Consultations

Irrespective of disease severity, over half of patients (53.0%) visited their consulting physician every 2–6 months, although patients with severe OA visited HCPs for OA-related reasons at a significantly higher mean rate than patients with mild or moderate OA (5.7 vs. 3.7 and 4.2 visits per year, respectively, all $p<0.05$). Patients with severe OA were more likely to consult a physician due to “deterioration of their OA condition” (32.4%), “continuing OA symptoms” (28.7%), or “current OA medication ineffective” (9.0%) than patients with mild OA (Supplementary Figure S2). These findings were also consistent with patients who had switched treatment regimens. In contrast, consultations for patients with mild/moderate OA were more likely to be routine follow-ups, requests for a repeat prescription, or for reasons unrelated to their OA ($p<0.01$;Supplementary Figure S2).

Disease severity dictated how patients were managed, with 70.0% of mild, 60.5% of moderate and 58.4% of severe OA patients consulting their PCP, while 25.1% of mild, 31.5% of moderate and 48.8% of severe OA patients consulted an orthopaedic surgeon, and rheumatologists saw 18.8% of mild, 29.2% of moderate and 26.7% of severe OA patients (Supplementary Table S1). Physicians reported significantly increased involvement of general practitioners, orthopaedic surgeons, pain specialists, nurse practitioners, radiologists, and physiotherapists in the management of severe patients relative to mild and moderate patients (all $p<0.05$).

Diagnostic and monitoring tests

Diagnosis

Diagnosis of OA involved a review of the patients’ medical history and a wide variety of tests and/or scans over the prior 12 months. C-reactive protein test, tender and swollen joint counts and measurements of blood pressure were the most frequently performed procedures/investigations. The most frequently performed imaging tests at diagnosis included X-ray, Magnetic Resonance Image (MRI) and Computed Tomography (CT) (Supplementary Figure S3a). In total, X-rays were performed at diagnosis in most patients (92.9% overall), with MRI and CT scans used in 19.7% and 8.8% of patients, respectively. The use of imaging to diagnose OA increased significantly with greater disease severity (all

p<0.05; Supplementary Figure S3a). Very few patients (4.2%) had no scans performed for diagnosis, the fewest in severe patients (2.4%) relative to mild and moderate (7.4% and 3.5%, respectively, *p*<0.05).

Monitoring

X-rays were the predominant scan used for disease monitoring, but the proportion of patients undergoing these scans for disease monitoring was lower compared to their use for diagnosis (62.3% vs. 92.9%) used in 49.0% of mild, 63.3% of moderate and 74.4% of severe OA patients (Supplementary Figure 3b). In total, 25.9% of patients did not receive a scan for disease monitoring, with the proportion of patients undergoing an x-ray for disease monitoring decreasing with greater disease severity (all *p*<0.05). The use of MRI and CT for disease monitoring increased with increasing disease severity in the overall population. MRI use for disease monitoring increased significantly across all disease severity groups (all *p*<0.05), and CT use was increased in severe patients relative to mild and moderate patients (*p*<0.05).

Hospitalisations

Inpatient hospital use was reported predominantly as part of surgical procedures for hip or knee replacement, or arthroscopic procedures. Physicians reported that OA patients with more severe disease were more likely to require a surgical procedure in the future (16.1% of mild, 41.9% of moderate and 69.7% of severe OA patients). Of the 711 patients (19.8%) for whom surgery was planned, significantly more patients with severe OA required a joint replacement (66.1%) compared with mild or moderate patients (both *p*<0.05).

Discussion

In this real-world point-in-time survey of physicians and their consulting OA patients, we found a clear association between physician-reported disease severity and treatment patterns and HCRU. Patients with more severe disease had greater use of non-pharmacological interventions and prescribed medication, with more frequent visits to HCPs, diagnostic and monitoring tests, and hospitalisations. Consistent with the findings of a similar survey in the US, patients and their physicians generally agreed on many of the factors associated with satisfaction with the medication prescribed for their OA, although the relative importance sometimes differed (28). Across Europe, pharmacological treatment patterns generally followed guideline recommended approaches, with paracetamol, NSAIDs and opioids the most frequently used medication classes in our OA patient cohort. However, a large proportion of physicians across Europe prescribed opioids for their patients with OA,

with almost half of all patients with severe OA prescribed an opioid medication, despite limited evidence for the benefit of opioids on OA symptoms and the international concerns about the devastating potential for dependency posed by opioid medications (15). The factors leading to the rising opioid prescription rates need to be better understood if clinical practice is to change (20).

In general, greater HCRU was observed among severe vs. milder OA patients in terms of the use of imaging tests for diagnosis and monitoring, visits to HCPs and hospitalisation, primarily for surgery. When needed, conventional radiography should be used before other modalities, such as MRI, CT or ultrasound (US) (11)). In line with guideline recommendations, X-rays were the most performed imaging for OA diagnosis and monitoring, and their use increased with greater disease severity. In only a small percentage of patients (4%), no imaging was performed for OA diagnosis, while MRI and CT were used in less than 20% of patients with no significant differences in diagnosis or monitoring between disease severities. Imaging using these modalities is suitable where there is unexpected disease progression of symptoms or a change in clinical characteristics and is not generally required for OA diagnosis (11).

Demand on HCRU, in terms of the number and type of tests or scans undertaken, which increased with greater disease severity, represents a large proportion of the overall economic cost of OA (29, 30), confirming the importance of considering disease severity in OA managementVisits to HCPs, another factor contributing to HCRU, also increased with greater disease severity. The reasons for the most recent visit also showed an association with disease severity: patients with severe vs. milder OA were more likely to consult physicians because of a deterioration in their OA, continuing OA symptoms, and ineffective OA medication.

Limitations

As our study was a point-in-time survey, no attempt was made to collect longitudinal data and therefore no causality can be established. In order to represent the real-world setting, the diagnosis of OA was based on the responding physician’s judgement and diagnostic skills rather than on a formalized diagnostic checklist, such that a level of subjectivity has to be considered when interpreting our results. In addition, since the patients were representative of those who were currently seeking treatment for their OA, there is a potential over-representation of well-motivated patients, or patients with less impaired mobility who were able to attend physician visits. Finally, the relatively small samples of patients stratified by affected joint location meant that the analysis was limited to HCP

consultations, diagnosis, monitoring, and provision of symptomatic relief by disease severity, irrespective of the site of OA.

Despite these limitations, our findings contribute to the current knowledge of treatment patterns and HCRU in the OA population in Europe from a large sample of more than 3,500 patients.

Conclusions

Across five European countries, patients diagnosed with severe OA experience higher HCRU, including imaging tests for diagnosis and monitoring, visits to HCPs and hospitalisation, which represent a large proportion of the overall economic cost of OA. Imaging was over-utilised, especially in diagnosis. Physicians are limited in their treatment options and are dissatisfied with current pharmacotherapy choice, most frequently due to inadequate response to medication and lack of improvement in the patient's quality of life, especially in patients with greater disease severity. As the treating physician has limited options, the same few therapies are cycled in subsequent treatment lines. The use of both pharmacological treatments and medication combinations increases with greater disease severity and almost half of all patients with severe OA are prescribed an opioid medication, despite limited evidence of its benefits and concerns over the long term risk of dependency.

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Tables

Table 1. Patient demographics by disease severity

	All patients (n=3,596)	Mild (n=874)	Moderate (n=1,904)	Severe (n=818)
Age, years, mean (SD)	66.4 (11.9)	62.4 (11.7)*†	66.7 (11.3)‡	70.2 (12.1)
Female, n (%)	2,107 (58.6)	472 (54.0)*†	1,148 (60.3)	487 (59.5)
Countries, n (%)				
France	672 (18.7)	92 (10.5)	396 (20.8)	184 (22.5)
Germany	743 (20.7)	276 (31.6)	344 (18.1)	123 (15.0)
Italy	671 (18.7)	169 (19.3)	360 (18.9)	142 (17.4)
Spain	747 (20.8)	133 (15.2)	417 (21.9)	197 (24.1)
UK	763 (21.2)	204 (23.3)	387 (20.3)	172 (21.0)
Ethnicity, n (%)				
White/Caucasian	3,301 (91.8)	813 (93.0)	1,736 (91.2)	752 (91.9)
Hispanic/Latino	106 (2.9)	19 (2.2)	62 (3.3)	25 (3.1)
Afro-Caribbean	67 (1.9)	12 (1.4)	45 (2.4)	10 (1.2)
Asian-Indian subcontinent	49 (1.4)	13 (1.5)	19 (1.0)	17 (2.1)
Middle Eastern	46 (1.3)	7 (0.8)	27 (1.4)	12 (1.5)
Other[a]	27 (0.8)	10 (1.1)	15 (0.8)	2 (0.2)
BMI, kg/m^2, mean (SD)[b]	27.3 (4.6)	26.3 (4.2)*†	27.4 (4.6)‡	28.0 (5.1)
Obese (≥30 kg/m^2), n (%)	836 (23.3)	139 (15.9)*†	456 (24.0)‡	240 (29.3)
Employment status, n (%)[c]				
Retired	1,914 (54.1)	367 (42.7)	1,032 (55.1)	515 (63.7)
Working full-time	818 (23.1)	288 (33.5)	421 (22.5)	109 (13.5)
Homemaker	439 (12.4)	100 (11.6)	233 (12.4)	106 (13.1)
Working part-time	229 (6.5)	75 (8.7)	115 (6.1)	39 (4.8)
Unemployed	75 (2.1)	17 (2.0)	39 (2.1)	19 (2.3)
On long-term sick leave	59 (1.7)	11 (1.3)	27 (1.4)	21 (2.6)
Student	6 (0.2)	1 (0.1)	5 (0.3)	0 (0.0)
Unemployed/retired due to OA, n (%)	99 (2.8)	11 (1.3)	43 (2.3)	45 (5.5)

[a]Other included Asian – other, Chinese, mixed race and patients describing their ethnicity as “other”
[b]Overall n=3,596
[c]Overall n=3,540
*p<0.05 vs. moderate
†p<0.05 vs. severe
‡p<0.05 vs. severe
BMI, body mass index; OA, osteoarthritis; SD, standard deviation.

Table 2. Patient clinical characteristics by disease severity

	All patients (n=3,596)	Mild (n=874)	Moderate (n=1,904)	Severe (n=818)
Comorbidities[a], n (%)				
Hypertension	1755 (48.8)	334 (38.2)*†	935 (49.1)‡	486 (59.4)
Diabetes	578 (16.1)	82 (9.4)*†	304 (16.0)‡	192 (23.5)
Dyslipidaemia/high cholesterol	504 (14.0)	97 (11.1)*†	265 (13.9)‡	142 (17.4)
Anxiety	431 (12.0)	76 (8.7)*†	232 (12.2)‡	123 (15.0)
Depression	392 (10.9)	63 (7.2)*†	199 (10.5)‡	130 (15.9)
Chronic lower back pain	345 (12.6)	41 (7.2)	165 (11.2)	139 (20.0)
Time since confirmed OA diagnosis, n	2,080	619	1,088	373
Mean (SD) years	3.5 (5.3)	2.6 (4.4)*†	3.7 (5.5)‡	4.5 (5.8)
Mean (SD) number of OA-affected joints	2.6 (2.1)	2.2 (1.6)*†	2.7 (2.1)‡	3.0 (2.5)
Currently affected joints, n (%)				
Knee	2005 (55.8)	421 (48.2)*†	1092 (57.4)	492 (60.1)
Hip	1221 (34.0)	237 (27.1)*†	618 (32.5)‡	366 (44.7)
Back	854 (23.7)	134 (15.3)*†	462 (24.3)‡	258 (31.5)
Hand/fingers	595 (16.5)	133 (15.2)*	352 (18.5)‡	110 (13.4)
Shoulder	483 (13.4)	124 (14.2)	244 (12.8)	115 (14.1)
Neck	392 (10.9)	69 (7.9)*†	210 (11.0)‡	113 (13.8)
Thumbs	334 (9.3)	69 (7.9)*	203 (10.7)‡	62 (7.6)
Wrist	267 (7.4)	81 (9.3)*†	132 (6.9)	54 (6.6)
Foot	187 (5.2)	43 (4.9)	105 (5.5)	39 (4.8)
Ankle	141 (3.9)	37 (4.2)	77 (4.0)	27 (3.3)
Elbow	106 (2.9)	39 (4.5)*†	48 (2.5)	19 (2.3)
Site of previous surgery, n (%)	147	40	53	54
Hip replacement	33 (22.4)	12 (30.0)	7 (13.2)	14 (25.9)
Knee replacement	69 (46.9)	19 (47.5)	26 (49.1)	24 (44.4)
Hand/thumb/finger/wrist/elbow	7 (4.8)	2 (5.0)	2 (3.8)	3 (5.6)
Charlson Comorbidity Index score, mean (SD)	0.4 (0.9)	0.3 (0.6)*†	0.4 (0.8)‡	0.7 (1.1)
Physician-reported current pain level, mean (SD)[b]	5.0 (2.1)	3.1 (1.6)	5.1 (1.7)	6.9 (1.7)
Physician-reported current function, mean (SD)[c]	4.8 (2.3)	3.1 (2.2)*†	4.8 (2.0)‡	6.6 (1.9)

[a]Comorbidities affecting less than 10% of the overall population not listed here
[b]Measured on scale 0-10 (0=no pain, 10=worst imaginable pain)
[c]Measured on scale 0-10 (0=completely functional, 10=completely impaired)
*p<0.05 vs. moderate
†p<0.05 vs. severe
‡p<0.05 vs. severe
OA, osteoarthritis; SD, standard deviation

Table 3. Prescription drug treatment history by disease severity[a]

	All patients	Mild	Moderate	Severe
Initial regimen, n	3019	697	1619	703
Number of classes, mean (SD)	1.6 (0.8)	1.4 (0.6)	1.5 (0.7)‡	1.8 (0.9)
Monotherapy, n (%)	1803 (59.7)	511 (73.3)*†	966 (59.7)‡	326 (46.4)
NSAID	1034 (34.2)	326 (46.8)*†	548 (33.8)‡	160 (22.8)
Paracetamol	485 (16.1)	112 (16.1)†	284 (17.5)‡	89 (12.7)
Opioid	161 (5.3)	31 (4.4)†	81 (5.0)‡	49 (7.0)
Corticosteroid	55 (1.8)	18 (2.6)*†	25 (1.5)	12 (1.7)
Glycosaminoglycan (e.g. glucosamine, chondroitin)	41 (1.4)	14 (2.0)*†	20 (1.2)	7 (1.0)
Viscosupplement (e.g. hyaluronic acid)	27 (0.9)	11 (1.6)*†	13 (0.8)	6 (0.9)
Dual therapy, n (%)	913 (30.2)	154 (22.1)*†	513 (31.7)‡	246 (35.0)
Paracetamol + NSAID	411 (13.6)	66 (9.5)*†	240 (14.8)	105 (14.9)
Paracetamol + opioid	173 (5.7)	31 (4.4)*†	91 (5.6)‡	51 (7.3)
NSAID + opioid	133 (4.4)	21 (3.0)*†	66 (4.1)‡	46 (6.5)
Other combinations	196 (6.5)	36 (5.2)	116 (7.2)	44 (6.3)
3+ drug treatments, n (%)	302 (10.0)	32 (4.6)*†	139 (8.6)‡	131 (18.6)
Paracetamol + NSAID + opioid	105 (3.5)	15 (2.2)†	45 (2.8)‡	45 (6.4)
Paracetamol + NSAID + glycosaminoglycan	39 (1.3)	4 (0.6)†	16 (1.0)‡	19 (2.7)
Paracetamol + NSAID + corticosteroid	25 (0.8)	1 (0.1)*†	18 (1.1)	6 (0.9)
Other combinations	134 (4.4)	12 (1.7)*†	61 (3.8)‡	61 (8.7)
Second regimen (1st switch), n	1524	190	887	447
Reason for switch – lack of efficacy, n (%)	1079 (70.8)	111 (58.4)*†	627 (70.7)‡	341 (76.3)
Number of classes, mean (SD)	1.9 (0.9)	1.6 (0.7)	1.8 (0.8)	2.0 (0.9)
Monotherapy, n (%)	616 (40.4)	104 (54.7)*†	370 (41.7)‡	142 (31.8)
NSAID	320 (21.0)	52 (27.4)*†	202 (22.8)‡	66 (14.8)
Paracetamol	135 (8.9)	31 (16.3)*†	75 (8.5)‡	29 (6.5)
Opioid	102 (6.7)	10 (5.3)*	63 (7.1)	29 (6.5)
Corticosteroid	34 (2.2)	7 (3.7)	16 (1.8)	11 (2.5)
Glycosaminoglycan (e.g. glucosamine, chondroitin)	13 (0.9)	4 (2.1)	6 (0.7)	3 (0.7)
Viscosupplement (e.g. hyaluronic acid)	12 (0.8)	0 (0.0)	8 (0.9)	4 (0.9)
Dual therapy, n (%)	640 (42.0)	69 (36.3)*†	372 (41.9)	199 (44.5)
Paracetamol + NSAID	204 (13.4)	18 (9.5)*†	123 (13.9)	63 (14.1)
NSAID + opioid	147 (9.6)	13 (6.8)*†	77 (8.7)‡	57 (12.8)
Paracetamol + opioid	135 (8.9)	13 (6.8)*†	77 (8.7)	45 (10.1)
Other dual combinations	154 (10.1)	25 (13.2)*†	95 (10.7)‡	34 (7.6)
3+ Drug treatments, n (%)	268 (17.6)	17 (2.4)*†	145 (16.3)‡	106 (23.7)
Paracetamol + NSAID + opioid	84 (5.5)	11 (5.8)*†	37 (4.2)‡	36 (8.1)
Paracetamol + NSAID + glycosaminoglycan	24 (1.6)	0 (0.0)*†	16 (1.8)	8 (1.8)
NSAID + opioid + corticosteroid	18 (1.2)	0 (0.0)*†	12 (1.4)	6 (1.3)
Other combinations	142 (9.3)	6 (3.2)*†	80 (9.0)‡	56 (12.5)

	All patients	Mild	Moderate	Severe
Third regimen (2nd switch), n	452	37	235	180
Reason for switch – Lack of efficacy, n (%)	344 (76.1)	21 (56.8)*†	172 (73.2)‡	151 (83.9)
Number of classes, mean (SD)	2.1 (1.0)	1.9 (1.1)	2.1 (1.0)	2.2 (1.0)
Monotherapy, n (%)	151 (33.4)	18 (48.6)*†	83 (35.3)‡	50 (27.8)
Opioid	46 (10.2)	2 (5.4)*†	23 (9.8)	21 (11.7)
NSAID	43 (9.5)	9 (24.3)*†	23 (9.8)	11 (6.1)
Paracetamol	43 (9.5)	6 (16.2)*†	23 (9.8)	14 (7.8)
Corticosteroid	10 (2.2)	0 (0.0)*†	7 (3.0)	3 (1.7)
Viscosupplement (e.g. hyaluronic acid)	6 (1.3)	0 (0.0)*	6 (2.6)‡	0 (0.0)
Glycosaminoglycan (e.g. glucosamine, chondroitin)	3 (0.7)	1 (2.7)*†	1 (0.4)	1 (0.6)
Dual therapy, n (%)	160 (35.4)	7 (18.9)*†	89 (37.9)	64 (35.6)
Paracetamol + Opioid	44 (9.7)	2 (5.4)*†	19 (8.1)‡	23 (12.8)
NSAID + Opioid	43 (9.5)	2 (5.4)*†	20 (8.5)‡	21 (11.7)
Paracetamol + NSAID	30 (6.6)	0 (0.0)*†	21 (8.9)‡	9 (5.0)
Other combinations	43 (9.5)	3 (8.1)*†	29 (12.3)‡	11 (6.1)
3+ Drug treatments, n (%)	141 (31.2)	12 (32.4)*†	63 (26.8)‡	66 (36.7)
Paracetamol + NSAID + Opioid	42 (9.3)	3 (8.1)†	17 (7.2)‡	22 (12.2)
NSAID + Opioid + Corticosteroid	15 (3.3)	0 (0.0)*†	3 (1.3)‡	12 (6.7)
Paracetamol + NSAID + Glycosaminoglycan	13 (2.9)	6 (16.2)*†	6 (2.6)	1 (0.6)
Other combinations	71 (15.7)	3 (8.1)*†	37 (15.7)	31 (17.2)

[a]1.5% of patients (n=53) received a fourth regimen but are not included in the above table
*p<0.05 vs. moderate
†p<0.05 vs. severe
‡p<0.05 vs. severe
NSAID, nonsteroidal anti-inflammatory drug; SD, standard deviation

Supplementary Table S1. Current non-pharmacological therapy (%) in patients with OA across five European countries

	Overall	France	Germany	Italy	Spain	UK
Avoiding any painful activities	36	38	44	24	29	32
Massage	31	32	41	24	26	17
Losing weight	29	26	12	31	52	41
Non weight-bearing exercise (e.g. swimming)	26	28	17	29	35	32
Weight-bearing exercise (e.g. walking, jogging)	23	24	15	21	29	32
Special insoles/cushioning in your shoes	10	19	3	8	13	10
Use of thermotherapy (ice or heat therapy)	9	8	9	7	14	7
Seeing a psychotherapist or counsellor	9	1	22	2	1	5
Taking dietary supplements	8	7	12	11	5	5
Acupuncture	8	7	10	3	7	10
Using home remedies	8	6	11	6	8	5
Yoga/Pilates	4	4	1	3	6	5
TENS	2	1	1	9	2	3

TENS, transdermal electrical nerve stimulation

Supplementary Table S2. Current class of prescription drug use (%) in patients with OA across five European countries

Prescription drug class	**Overall**	**France**	**Germany**	**Italy**	**Spain**	**UK**
NSAID	64	49	86	72	55	55
Paracetamol	46	63	11	30	60	66
Any opioid	38	33	25	32	49	51
Weak opioid	28	30	13	19	33	46
Corticosteroids	10	13	12	10	7	10
Glycosaminoglycans	10	15	4	9	20	1
Strong opioid	10	2	12	12	16	5
Viscosupplements	6	16	2	7	5	0
Opioid + analgesic (combined tablet)	1	1	0	2	1	1

NSAID, non-steroidal anti-inflammatory drug

OPTIONAL Supplementary Table S3. Current prescription drug use (%) in patients with OA across five European countries

Prescription drug	Overall	France	Germany	Italy	Spain	UK
Any NSAID	62	47	85	70	53	53
Paracetamol	44	62	5	30	59	66
Any opioids	37	33	23	32	48	50
Combination opioids	30	27	18	24	40	41
Weak opioids	26	30	10	19	32	39
Tramadol	18	20	10	14	31	12
Ibuprofen	15	7	22	14	11	18
Celecoxib	13	14	16	14	16	3
Diclofenac	13	15	17	21	3	8
Strong opioids	11	2	13	12	16	10
Etoricoxib	10	1	16	18	12	3
Intra-articular corticosteroid	9	12	11	8	7	10
Codeine	9	10	0	5	1	29
Naproxen	8	7	5	5	7	18
Chondroitin	7	11	2	5	15	0
Glucosamine	5	7	3	7	8	1
Hyaluronic acid	5	15	2	6	5	0
Naproxen/esomeprazole	3	3	6	1	3	3
Tapentadol	3	0	3	6	6	0
Oxycodone	3	1	4	4	4	1
Fentanyl	2	1	3	1	5	1
Meloxicam	2	2	4	2	2	1
Buprenorphine	1	0	1	0	1	5
Morphine	1	1	2	0	1	3
Hydrocodone/paracetamol	1	0	0	2	1	0
Dihydrocodeine	1	0	0	0	0	3

NSAID, non-steroidal anti-inflammatory drug

Figures

Figure 1. Non-pharmacological interventions by disease severity

*$p<0.05$; mild vs. moderate
†$p<0.05$; mild vs. severe
‡$p<0.05$; moderate vs. severe
TENS, transcutaneous electrical nerve stimulation

Figure 2: Current (A) and previous (B) pharmacological treatment by disease therapy

NSAID, nonsteroidal anti-inflammatory drug

Figure 3 Top six therapies by treatment line

NSAID, nonsteroidal anti-inflammatory drugs; COX-2 inhibitor, cyclooxygenase-2 inhibitor