INTRODUCTION

Osteoarthritis (OA) is a progressive chronic disease potentially affecting every articular tissue and may potentially lead to joint failure. It has heterogeneous manifestation and, does not always have the same appearance in all patients. Indeed, OA may present differently in men and women, in patients with or without trauma, in athletes, or in obese patients [1,2]. OA articular cartilage changes result from the disruption of the normal balance between anabolic and catabolic processes, as well as cellular abnormalities in autocrine, paracrine, and endocrine regulation, leading to a disequilibrium in normal tissue turnover within the joint [2].

Numerous factors have been associated with an increased risk for the development of OA. These include systemic factors such as genetics, age and gender, sex hormones, bone mineral density, as well as local mechanical factors such as joint overload caused by obesity, acute injury, repetitive joint loading, and joint deformity [3]. Despite the multifactorial nature of OA, the pathological changes seen in osteoarthritic joints have common features that affect the entire joint structure resulting in pain, deformity, and loss of function [4].

OA can be defined in terms of radiologic changes as well as symptoms, although there may be a discordance between these findings since many people with pathologic and radiographic evidence of osteoarthritis have no symptoms [5]. From a clinical perspective, pain is the disease characteristic that negatively affects multiple aspects of patient’s life, including mobility, sleep, mood, and health related quality of life (HRQoL) [6]. Pain and function

ABSTRACT

OBJECTIVE: To determine how osteoarthritis (OA) severity correlates with self-reported outcomes relevant from the patient’s perspective in the Italian clinical setting.

METHODS: Data were drawn from the 2017-18 Adelphi OA Disease Specific ProgrammeTM (DSP). Data were collected in the Italian clinical practice settings by primary care physicians, rheumatologists, orthopedists, and their patients with OA, during their regular office visits. Physicians completed information about OA-related visits to healthcare professionals (HCPs), tests/scans conducted, emergency room (ER) visits, surgeries, and OA-related treatment. Physicians also rated patients’ functioning on a 0 to 10 scale (0 = fully functional; 10 = completely impaired). Outcomes included Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, functional limitations, treatment needs, EuroQoL-5 Dimension (EQ-5D) visual analogue scale (VAS), the work productivity and activity impairment. Descriptive statistics (numbers and percent for categorical variables; means with standard deviations [SD] for continuous variables) were used to evaluate the different variables as appropriate.

RESULTS: The study population comprised 900 patients from Italy with knee (40.9%), back (38.7%), hip (27.9%), and/or shoulder (20.3%) OA. Mean age was 66.6 years with a prevalence of female (63%) patients. Patients had mild (26%), moderate (54%), severe (20%) disease severity. Patients with severe disease reported higher functional limitations, greater use of treatments, reduced quality of life, and impaired work productivity and activity. The burdens were higher among elderly and obese patients and in patients with highest pain severity score.

CONCLUSIONS: The results from this cross-sectional study show the impact of OA disease severity on all dimensions of health-related quality of life (HRQoL), as well as in OA-related health care resource use.

Keywords

Daily activity; Health-related quality of life; Osteoarthritis; Pain; Physical functioning; Work productivity
are core symptomatic outcomes of OA that are frequently targeted as part of pharmacologic therapy, and it may be expected that these outcomes are associated with patient perceptions of OA severity [7].

A variety of pharmacologic options are available for managing OA-related pain such as simple analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), oral corticosteroids, opioids, and injectables including corticosteroids and viscosupplementation with hyaluronan [8]. As occurs with most chronic conditions, adherence to OA medications is low. Factors implicated in adherence to OA include dosing frequency, self-efficacy levels, and physician and patient treatment satisfaction [9].

While simple analgesics and NSAIDs are generally recommended as first-line pharmacologic therapy, in clinical practice choosing among these medications is often determined by disease severity [10]. In clinical trials, definitions of severity are generally based on cut-points for patient-reported pain, function, and global assessments. However, in real-world settings, categorizing mild, moderate, or severe disease based solely on pain cut-points may be neither comprehensive nor relevant from the patient’s perspective. Other factors such as functional impairment and work productivity may also contribute to a patient’s overall perception of disease severity [11,12]. As a result, patients with OA report impairment of their ability to carry out activities of daily living in addition to deterioration in HRQoL.

As a consequence, OA patients are very high users of health care services and incur higher costs than patients without OA, due to the duration of disease and the level of impairment related to their illness [13]. The burden of OA is therefore considerable, both from a societal and individual patient perspective [14]. OA is responsible for a very high number of primary healthcare visits as well as knee and hip replacement procedures, plus hospital admission costs, as well as assistance for follow-up and rehabilitation [15]. However, the socio-economic burden of OA is not only limited to the direct costs of healthcare use, but also includes significant non-healthcare-related costs. These take the form of productivity losses and the cost of formal and informal care associated with the limited independence of people with osteoarthritis [15].

Considering Disability Adjusted Life Years (DALYs) over the period 1990-2010, OA burden of disease has grown at a faster pace than musculoskeletal diseases (64% vs 45%) [16]. According to the Italian Health Ministry, OA resulted to be the 7th out of 283 diagnosis for Clinical Classifications Software (CCS) for number of hospital discharges from hospital data collected in 2014 [16]. Hospital discharges for OA in Italy were 127,000, close to the 2% of the discharges with an average hospital stay of 7.5 days [17]. In Italy annual total costs per patient have been estimated €3,000 (€1,300 as direct health-related costs and €1,700 as indirect costs adjusted in 2013) [18]. Recently, Berto and Aiello conducted a literature review, revealing that the impact of OA on the Health System, generates direct health costs related to hospital admissions for hip and knee surgery; and may generate additional costs due to relapses, need for intervention review, adverse events (e.g., infections, thrombosis and pulmonary embolisms) and subsequently to the rehabilitation process, in hospital and at home. They also reported the burden of illness also generated by indirect costs characterized by the reduced or lack of productivity of patient and family members, as patients with OA are affected by severe limitations in daily and work activities [19].

Overall, OA is a chronic condition that impacts significantly on life expectancy and patients’ HRQoL and generates considerable costs to most health care systems. As with any chronic condition, non-adherence to the available pharmacological treatments is a problem that has the potential to impact on population health and expenditure.

Given that OA exerts multiple effects on patients’ lives, the objective of this study was to determine how patient-rated OA severity (mild, moderate and severe) can affect self-reported outcomes relevant from the patient’s perspective, including assistance with mobility and daily activities. Additionally, this study aims to understand the pattern of healthcare resource utilization (HCRU) in Italy as OA severity worsens.

METHODS

Study Design

This study utilized data from the 2017-18 Osteoarthritis Adelphi Disease Specific Programme (DSP)™. The Adelphi DSP is a large, multinational, point in time survey designed to capture a cross-section of real-world data for a range of common chronic diseases [20]. Data were collected in Italian clinical practice settings from primary care physicians, rheumatolo-
gists, orthopedists, and their patients with OA, during their regular office visits. Physicians completed patient record forms (PRFs) on their next 9 consecutive patients ≥18 years) consulting for OA, plus an oversample of 1 patient who had tried at least 3 prescribed medications for their OA pain. These patients were also invited to participate by providing written informed consent and completing a patient self-completion questionnaire (PSC). Physicians completed information about OA-related visits to healthcare professionals (HCPs), tests/scans conducted, emergency room (ER) visits, surgeries, and OA-related treatment. Physicians also rated patients’ functioning on a 0 to 10 scale (0 = fully functional; 10 = completely impaired).

OA pain intensity and physical function were measured using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), a widely used, validated, self-administered, disease-specific questionnaire [21]. Patients rated their average pain intensity over the last week on a 0-10 scale (0 = no pain; 10 = worst possible pain) and, using the pain component of the WOMAC, were categorized into mild (0-3), moderate (4-6) and severe (7-10) pain groups.

Patients also provided an assessment of their physical function (0-10 WOMAC scale where higher scores indicated greater functional impairment), impact on mobility, whether caregiver assistance was required, and daily activities requiring caregiver assistance.

The analysis was conducted using combined data from the total patient sample (random sample + over-sample). Not all physicians and patients answered all the questions on the PRF and PSC, respectively. Consequently, the respondent population size may differ for individual questions and thus for certain analyses. The population size is given for each individual analysis where appropriate and indicates the number of respondents (physician or patient) who provided responses relevant to that analysis.

Outcome Measures

Outcomes included measures for physical functioning, HRQoL, pain, work productivity and daily activity. Physical functioning was reported by patients using pain, physical function and stiffness scores from the WOMAC which are scored on a range from 0 to 10. Generic HRQoL was assessed using the EuroQol-5 Dimension (EQ-5D) instrument [22]. The EQ-5D includes a separate visual analogue scale (VAS) which varies from 0 = worst health you can imagine to 100 = best health you can imagine [22]. Work productivity and daily activity were assessed using the patient-reported Work Productivity and Activity Impairment Questionnaire (WPAI). WPAI scores are based on 1-item (presenteeism, activity impairment), 2-items (absenteeism) and multiple items (overall work productivity).

Statistical Analysis

Descriptive statistics (numbers and percent for categorical variables; means with standard deviations [SD] for continuous variables) were used to evaluate the different variables as appropriate.

RESULTS

Demographic and Clinical Characteristics

A total of 90 physicians were included in the analysis. Physicians’ specialties were primary care (50), orthopedists (30) and rheumatologists (10). Each physician included 10 patients: 500 patients from primary care, 300 patients from orthopedists and 100 patients from rheumatologists providing data for a total of 900 patients. Physicians provided information from patient records on patient demographics and clinical characteristics including the random sample as well as the over-sample.

As shown in Table I, which presents the demographic characteristics, individuals were predominantly female (63%) and the mean age was 66.6 years (SD 12.4). The mean body mass index (BMI) was 26.3 (SD 3.8), with 25% of patients being reported as obese (BMI>30) by physicians. There was a high presence (46.5%) of patients who were retired, and about one third (32.1%) were employed (25.9% in full time, 6.2% in part-time employment). Only 3% of patients reported being retired due to OA.

Among the study sample, 237 (26%) patients were classified by physicians as having mild OA, 482 (54%) moderate OA and 181 (20%) had severe OA (Table I). Among 900 patients, 699 (129 %) patients reported additional conditions on top of their OA. The most frequently were cardiovascular conditions (66%), neurological conditions (33%) and diabetes/endocrine diseases 32% (Table I).
As to the clinical profile 7% of patients were classified as rapidly deteriorating, 38% as slowly deteriorating, 45% were reported as having a stable disease and 10% as currently improving their disease status. Joints mostly affected by OA were the knee (40.9%) and the back (38.7%) followed by the hip (27.9%) and the shoulder (20.3%), with relatively lower frequencies for the hand, neck and wrist. Looking at patient’s functionality, as recorded by the treating physician, patients appeared to stand on the higher area of the spectrum, with 43% of patients being rated 6 or higher (on a scale 0-10 where 0 implies full functionality and 10 complete impairment) (Table I).

The average number of OA-related visits to the physician reported in the past 3 months by patients was 3.75 and an additional 1 visit was reported to a different health care professional (HCP) (on average, about 19/year). The average number of medical and other HCP visits appeared higher in the elderly (age group 74-89), in patients with higher pain severity (NRS 7-10) and in severe patients (according to both patients’ and physicians’ assessed disease severity) (Supplementary Figure 1). Severe patients reported respectively 24.3 and 22.3 visits per year (severity assessed by patients and physicians, respectively).

### Prescribed OA Treatment Patterns

Exposure to pain-related treatments among OA patients was assessed in relation to disease progression, disease severity and pain severity.

Duration of treatment was the lowest in patients deteriorating rapidly; in (both rapidly and slowly) deteriorating patients on average 2 classes of drugs were used. The highest rate of strong opioids (46%) and analgesics (38%) use was recorded in patients deteriorating rapidly. In stable and improving patients, strong opioids were used only by a minority of patients (7% and 5%, respectively) (Figure 1).

No difference in duration of treatment by severity of disease was reported. Severe patients were prescribed 2 classes of drugs (vs 1 in mild and moderate patients); severe patients were more likely to be prescribed strong opioids (37%), weak opioids (26%) and analgesics (32%), whilst moderate patients used more NSAIDs (74%), but still one in five (20%) of moderate patients used weak opioids (Figure 2).

Duration of treatment by severity of pain (NRS 0-10), revealed no differences although there seemed to be a tendency towards a longer treatment duration with the decrease of pain severity. Severe pain patients (NRS 7-10) and moderate pain patients (NRS 4-6) used 2 classes of drugs (vs 1 in mild pain patients NRS 0-3); severe pain patients used more of all classes

<table>
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<tr>
<th>Characteristic</th>
<th>Value</th>
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<tr>
<td>Mean age, years (n=900)</td>
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<td>Gender, % M/F (n=889)</td>
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<td>BMI (n=899)</td>
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<td>Deteriorating rapidly</td>
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<td>Knee</td>
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Table I. Demographics and clinical characteristics of patients with OA
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**Figure 1. Drug classes by disease progression**

1 Non-opioid / non-NSAID

2 Other include: Corticosteroids, Opioid Combination, Viscosupplements, Glycosaminoglycans, Other Analgesic, Immunosuppressant, Monoclonal antibodies, Antidepressants, Anticonvulsant, Disease modifying antirheumatic drugs (DMARD), Bisphosphonate

**Figure 2. Drug classes by disease severity**

1 Non-opioid / non-NSAID

2 Other include: Corticosteroids, Opioid Combination, Viscosupplements, Glycosaminoglycans, Other Analgesic, Immunosuppressant, Monoclonal antibodies, Antidepressants, Anticonvulsant, Disease modifying antirheumatic drugs (DMARD), Bisphosphonate

except NSAIDs, which still represent the drug class mostly used in all groups, with consumption being particularly higher in mild and moderate pain patients (Figure 3).

On average, across all patient subgroups about 44% of patients progressed to a second line, 19% to a third line and only 2% progressed to a fourth line of treatment, with a ten-
In patients whose disease was classified as mild only a minority progressed to second (26%), third (10%) and fourth (1%) line of treatment. Most used treatment classes in mild patients were NSAIDs and analgesics with a very limited number of cases in which both weak and strong opioids were used (in second and third line of treatment) (Supplementary Figure 2).

In moderate patients about 43% of subjects progressed to a second line, 17% to a third line and less than 1% progressed to a fourth line of treatment, with a tendency to added weak and strong opioids. 67% of patients classified as severe progress to second line, 31% of patients progressed to third and 7% to fourth line of treatment; percentage transitions across treatment lines in severe patients were the highest (so severe patients show to be treated with more drugs and more treatment lines than any other severity group). Also, in severe patients there was a wider use of strong opioids, especially in patients progressing to the third and fourth line of treatment. Of note, in severe patients the mean pain score was 7, irrespective of treatment line.

Physicians reported their satisfaction with treatment in relation to 651 patients for which a full treatment regimen was recorded (Supplementary Figure 3). In 26.6% of cases (n=173) they reported being dissatisfied (this includes Neither satisfied nor dissatisfied; Somewhat dissatisfied; Very dissatisfied). Among these 173 cases, reasons for dissatisfaction were investigated, with physicians reporting that in 37% of cases they find inadequate response and in 27% lack of improvement in patient quality of life; another 12% of dissatisfaction reports can be attributed to side effects (notably local reactions to injections; severity of side effects suffered; number of side effects suffered).

Patients reported their satisfaction with OA treatment(s) (Supplementary Figure 4). In 51% of cases (n=114) they reported being dissatisfied (this includes Neither satisfied nor dissatisfied; Somewhat dissatisfied; Very dissatisfied). Dissatisfaction with treatment seems more marked in the elderly (≥74 years old) (64%), obese patients (65%), and in severe patients as assessed by both patients (81%) and physicians (69%).

Patients reported on OA-related surgeries (Supplementary Figure 5). The average incidence of surgery was 14% in all patients (n=242), with higher percentages reported by patients in the oldest age group (24%), by obese (BMI>30) vs non obese patients (32% vs 10%), by patients reporting severe pain (25%), and by patients classified as severe according to both patient’s (31%) and physician’s (26%) disease severity assessment.

Figure 3. Drug classes by pain severity

1 Non-opioid /non-NSAID
2 Other include: Corticosteroids, Opioid Combination, Viscosupplements, Glicosaminoglycans, Other Analgesic, Immunosuppressant, Monoclonal antibodies, Antidepressants, Anticonvulsant, Disease modifying antiinflammatory drugs (DMARD), Bisphosphonate
Physical Functioning

Physical functioning was reported by patients using pain, physical function and stiffness scores from the WOMAC, each on a scale 0-10 (Figure 4). In the total population, patients classified as severe, according to physician’s and patient’s disease severity assessment, reported WOMAC score 19.8 and 18.9, respectively. In addition, a higher WOMAC score was reported in elderly (age 74-89) and obese (BMI>30) patients, 16.1 and 15.9, respectively.

Mobility limitation, need for a walking aid, need for help with daily activities, and suffering a fall were assessed by patient responses to stand-alone questions related to functional limitations.

Among 239 patients, 141 (59%) reported that OA had an impact on physical mobility which seems to affect mostly patients in older age cohorts (63-73 and 74-89) with impairment reported by 67% and 83% of patients, respectively. Higher rate of mobility limitation was noted in obese patients (71%) and, in patients with moderate and severe disease severity, according to patients’ severity assessment (66% and 88% respectively) as well as according to physicians’ severity assessment (66% and 83% respectively) (Supplementary Figure 6).

Patients reported their need help for getting around (Supplementary Figure 7). On average, 29% reported they need a cane/walking stick, 3% they need a walking frame, 1% reported they need a wheelchair. Higher percentages were recorded by patients in the older age class; male patients (42% of them need cane/walking stick), obese patients (in total 59% of them need some sort of support) and severe patients according to patients’ disease severity assessment (48% need support) as well as according to physicians’ severity assessment (52% need support).

22% of 237 patients (about one in five individuals) reported that OA generates the need for some help with daily activities or tasks (Supplementary Figure 8). This seems to affect mostly the elderly (74-89) with external need reported by 48% of patients, obese patients (BMI>30) with 36%, patients with longer disease duration with reported 24%, and severe patients according to patients’ disease severity assessment (47%) as well as according to physicians’ severity assessment (46%).

Patients reported on falls attributed to OA. As shown the average incidence of falls was 21% in all patients (n=244) with higher percentages reported by patients in the oldest age group (21%), by women vs men (23% vs 17%), by obese (BMI>30) vs non obese patients (28% vs 19%), by patients reporting severe pain (49%), and by patients classified as severe according to both patient’s (40%) and physician’s (32%) disease severity assessment (Supplementary Figure 9).

A total of 62 patients reported on the number of hours per week that family, friends or professional caregivers provided to help care (Supplementary Figure 10). Patients were as-
Osteoarthritis in Italy: Impact on Health-Related Quality of Life and Health Care Resources

sisted for about 13.6 hours/week on average. Patient groups that required more assistance were those in the 65-73 age category (17.9 hrs/wk), obese patients (30.3 hrs/wk), patients with higher pain score (20.6 hrs/wk) and patients classified as severe according to both patient’s (21.7 hrs/wk) and physician’s (17.0 hrs/wk) disease severity assessment.

**HRQoL**

HRQoL, assessed by the EQ-5D-5L VAS recorded the patient’s self-rated health on a vertical visual analogue scale, where the endpoints are labelled ‘The best health you can imagine’ and ‘The worst health you can imagine’ (Figure 5). Patients scored their health at an average of 62.5 with lower scores being recorded for the elderly (52.2), patients with the highest pain severity (53.5) and for patients being classified as severe, according to both physicians (47.8) and patients (51.1) disease severity assessment.

**Work Productivity and Daily Activity**

WPAI score on the overall work productivity was collected on 237 subjects (Figure 6). On average OA patients reported their work productivity was impaired by 45% due to OA problems. Higher WPAI scores were reported by the oldest patients’ age group (58%), by obese patients (57%), by patients reporting more severe pain (66%) and by patients classified as severe according to both patient’s (71%) and physician’s (67%) disease severity assessment. Patients reported the effect of OA on their work productivity over the past 7 days, on a scale 0-10 (0=no effect; 10=completely preventing work) (Supplementary Figure 11). Mean score across all patients was 2.5; higher effect was reported by patients aged 65-73 years (5.0), female (2.9), obese patients (3.3) patients with duration of disease>1 year (3.2), patients with highest pain severity score (4.5) and patients classified as severe by both patient’s and physician’s assessment (score 5.4 and 4.5, respectively).

73 patients reported having missed on average 3.5 hours of work over the past 7 days, with the highest work loss recorded by patients aged 65-73 years (14 hours), male (6.4 hours), patients with highest pain severity score (12.9) and patients classified as severe by both patient’s and physician’s assessment (16.8 and 27 hours, respectively) (Supplementary Figure 12).

Almost all patients (n=237) reported on the effect of OA on their ability to perform daily activities over the past 7 days, on a scale 0-10 (0=no effect; 10=completely preventing activity) (Supplementary Figure 13). Mean score across all patients was 4.5; higher effect was reported by patients aged 74-89 years (5.8), obese patients (5.7), patients with highest pain severity score (6.6) and patients classified as severe by both patient’s and physician’s assessment (score 7.1 and 6.7, respectively).
DISCUSSION

In this cross-sectional study, Italian patients with severe OA disease severity reported significant burdens that affected multiple aspects of their lives, encompassing reductions in physical functioning, greater treatment needs, reduced HRQoL, and impairments in work productivity and daily activities.

The high prevalence of OA among the elderly is well known [23-25]. Age-related changes occurring in tissues besides articular cartilage may contribute to the development of OA and are much more intense in the presence of obesity [26]. In the current study, burdens affecting OA patients were higher among the elderly and obese individuals.

OA is associated with a significant functional impairment that can result in disability [27]. The results of this study demonstrated that at each level of OA severity, the corresponding magnitude of functional impairment was different, with the greatest impact reported by physicians and patients who rated OA as severe. Patients with severe OA disease were more likely than mild and moderate-patients to report impairment in physical function, pain, stiffness, specific needs such as for a walking aid or help with daily activities, help care and that they suffered a fall. These results are in line with several cross-sectional studies that found a relationship between disease severity and physical function [28-31].

In OA patients, HRQoL is negatively affected [32, 33]. In this study, HRQoL, as measured by the EQ-5D VAS was lower among patients classified as severe, according to both physician’s and patient’s disease severity assessment. HRQoL was also lower among patients with higher pain severity. A systematic review by Vitaloni et al. revealed a substantial impact on quality of life (QoL) in patients affected by knee osteoarthritis (KOA). All reviewed studies reported worse QoL in KOA patients when compared to a control group. When females were compared to males, females reported worse QoL. Obesity, as well as lower level of physical activity, were also reported with lower QoL scores [34].

Previous studies have demonstrated an association between OA and reduced work productivity and the ability to perform daily activities [35, 36] and such impairments were also reported by patients in this study. These impairments, as measured by the WPAI score, were associated with higher disease severity and pain levels. Work productivity and daily activity impairments were higher in patients with highest pain severity score and in patients classified as severe by both patient’s and physician’s assessment. This finding is consistent with the results of other studies in OA showing that pain and disease severity has a negative association with employment status and productivity, including both absenteeism and presenteeism [30, 31].

The current study revealed a higher medication burden among patients with OA, and a greater proportion of these patients who were prescribed potent drugs. Even if NSAIDs are
considered first-line treatment for OA, opioids were the most frequently prescribed medication class in this Italian patients’ population. There was a higher prescribing rate of strong and weak opioids in patients with severe pain as well as in patients whose OA was classified as severe by both patient’s and physician’s assessment. This high rate of opioid prescribing is in accord with other studies that have shown opioids to be the most frequently prescribed pain-related medications in patients with OA [37]. In particular patients with severe disease reported use of two treatment regimens for OA. Additionally, physicians reported treatment dissatisfaction related to inadequate response and lack of improvement in patient quality of life while dissatisfaction from patients seems more marked in the elderly, obese patients, and severe patients.

Across all classes of prescription medications, approximately only one third of OA patients reported being very or extremely satisfied with their current medication, presenting some relevant problems, such as poor compliance / adherence to the treatments. Kingsbury et al. showed that 42% of Italian OA patients considered themselves to be fully adherent to their medication [36] and, the most common classes of prescription medication were NSAIDs and COX-2 inhibitors [36,38].

Healthcare resource utilization relative to individuals with OA is responsible for a substantial proportion of the economic burden of OA. These resources include not only pharmacologic and other therapies related for OA, but also management of treatment-related complications and surgery/ rehabilitation [18,39-42]. In the current study, OA patients classified as severe reported higher percentages of OA-related surgeries. In Italy during 2015 were performed around 181,738 surgeries (56.3% relates to the hip, 38.6% knee, 3.9%, 0.3% and 0.9% respectively shoulder, ankle and other joints). Since 2001 to 2015, the average annual increase in the number of total interventions was 4.1% [43]. The incremental healthcare costs of people with osteoarthritis compared to those without the disease reaches a maximum when osteoarthritis-related surgery becomes necessary [15]. The main direct health-related cost driver is the total joint arthroplasty [44]. The socioeconomic burden of total joint arthroplasties generated additional costs due to relapses, need for intervention review, adverse events (e.g. infections, thrombosis, and pulmonary embolisms) and subsequently to the rehabilitation process, in hospital and at home [45]. The steady increase, year after year, of surgery incidence led costs to grow [45-47] and this is expected also for the next future, in an ageing population [46].

As in previous studies that reported high rates of healthcare utilization among OA patients in terms of number of visits to a health care provider and hospitalizations [18,29,38,48], in the current study patients with OA utilized outpatient resources including medical and other health care professional (HCP) visits. This resource utilization was higher in patients with higher pain severity and in patients classified as severe by both patient’s and physician’s assessment. In Italy hospitalization represented 40% of the medical costs and among different admissions, those in rehabilitative care were the most expensive due to a stay in hospital prolonged up to 50 days in patients operated for arthroprothesis [18].

Interpretation and extrapolation of these results are subject to study limitations. These limitations include study participation based on agreement by physicians and patients. It is therefore possible that individuals who participated may have characteristics and perceptions different from those who refused to participate, thereby introducing selection bias and reducing generalizability. In addition, we are unable to attribute linked causality between OA and reported outcomes, since it is possible that co-morbid conditions and other factors may have contributed in part to the differences described. Furthermore, statistical comparisons were not conducted between the patient groups limiting the analysis of relevant differences.

CONCLUSION

This real-world-cross-sectional study demonstrated an increase in the scoring for all dimensions of QoL as well as in the use of resources as OA disease severity worsened. The burdens were higher among severe patients versus moderate and mild patients. Novel therapeutic agents that improve OA symptom management may lead to significant healthcare resource utilization savings.

Funding
This study was sponsored by Pfizer and Eli Lilly and Company. The analysis was conducted independently by Adelphi Real World. All authors actively collaborated on the study design and interpretation of results; contributed in writing this paper; and have provided final approval of the submitted version.

Conflicts of interest
PB and MDS are consultants of Regulatory Pharma Net srl. JJ, MB, and JJ are employees of Adelphi Real World.
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Figure 1. Average number of OA-related medical visits in the past 3 months
BMI = Body mass index; DD = Disease duration; DS* = Disease Severity assessed by patient; DS** = Disease Severity assessed by physician; HCP = Health Care Professional; PS = Pain Severity
Figure 2. Treatment history by disease severity

1 (non-opioid /non-NSAID)
2 Other include: Corticosteroids, Opioid Combination, Viscosupplements, Gycosaminoglycans, Other Analgesic, Immunosuppressant, Monoclonal antibodies, Antidepressants, Anticonvulsant, Disease modifying antirheumatic drugs (Dmard), Bisphosphonate

Figure 3. 3A Physician’s satisfaction with treatment (n=651); 3B Reason for dissatisfaction (n=173)
Figure 4. Patient's satisfaction with treatment
BMI = Body mass of index; DD = Disease duration; DS* = Disease Severity assessed by patient; DS** = Disease Severity assessed by physician

Figure 5. Surgeries due to OA
BMI = Body mass of index; DD = Disease duration; DS* = Disease Severity assessed by patient; DS** = Disease Severity assessed by physician; PS = Pain Severity
**Figure 6. Impact on physical mobility**

BMI = Body mass of index; DD = Disease duration; DS* = Disease Severity assessed by patient; DS** = Disease Severity assessed by physician

**Figure 7. Use of walking aids**

BMI = Body mass of index; DD = Disease duration; DS* = Disease Severity assessed by patient; DS** = Disease Severity assessed by physician
Figure 8. Need for help in daily activity
BMI = Body mass index; DD = Disease duration; DS* = Disease Severity assessed by patient; DS** = Disease Severity assessed by physician

Figure 9. Falls
BMI = Body mass index; DD = Disease duration; DS* = Disease Severity assessed by patient; DS** = Disease Severity assessed by physician; PS = Pain Severity
Figure 10. Hours family and professional caregiver
BMI = Body mass of index; DD = disease duration; DS* = Disease Severity assessed by patient; DS** = Disease Severity assessed by physician; PS = Pain Severity

Figure 11. Work productivity
BMI = Body mass of index; DD = disease duration; DS* = Disease Severity assessed by patient; DS** = Disease Severity assessed by physician; PS = Pain Severity
Figure 12. Hours missed from work
BMI = Body mass of index; DD = disease duration; DS* = Disease Severity assessed by patient; DS** = Disease Severity assessed by physician; PS = Pain Severity

Figure 13. Ability to perform daily activities
BMI = Body mass of index; DD = disease duration; DS* = Disease Severity assessed by patient; DS** = Disease Severity assessed by physician; PS = Pain Severity
All (n=237)