CANCER PAIN & PALLIATIVE CARE SECTION

Long-Term Pain Management and Health Care Resource Use Among an Employed Population in Japan with Knee Osteoarthritis Combined with Low Back Pain

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Abstract

Objective. Assess long-term comorbidity burden and pain management patterns among working-age patients with knee osteoarthritis (KOA) only without low back pain (LBP) (KOA-noLBP) and patients with KOA plus LBP (KOA+LBP) in Japan. **Methods**. Retrospective claims data analyses were conducted on data from the Japan Medical Data Center (JMDC) database. Adult patients (≥40 years) with a diagnosis of knee osteoarthritis (KOA) (January 1, 2011–December 31, 2012) and 5 years of follow-up were evaluated. The first claim with a KOA diagnosis defined the index date. Longitudinal pain management patterns were assessed in both cohorts. **Results**. Overall, 1,828 patients met study criteria (717 with KOA-noLBP; 1,111 with KOA+LBP). The mean age of patients with KOA-noLBP was 52.1 years, and that of patients with KOA+LBP was 53.1 years, with more females in the KOA+LBP cohort (49.4% vs. 55.0%). Regardless of cohort, >90% of patients received pharmacological intervention during the 5-year follow-up period. The most common regimen first received was either topical or oral nonsteroidal anti-inflammatory drugs. A higher mean number of pharmaceutical treatments were received by patients in the KOA+LBP cohort (3.6) than by patients in the KOA-noLBP cohort (2.7) during the follow-up period. Regardless of cohort, most of the direct medical cost was derived from medication. **Conclusion**. This study demonstrates that a greater proportion of the JMDC population of working individuals with KOA were comorbid with LBP and received pain-related treatment in the long-term perspective relative to patients with KOA without LBP. Appropriate pain management for both KOA and LBP would be key for effective resource utilization in an aging society facing socioeconomic burdens

Key Words: knee osteoarthritis; low back pain; pain management; working-aged; HCRU; real world; Japan

Introduction

Knee osteoarthritis (KOA) is a widely prevalent, disruptive, chronic, and progressive joint disease characterized by the destruction of knee cartilage [1, 2]. Previous studies have reported that as much as 30% of the worldwide population 50 years of age and above suffers from KOA [3, 4]. An observational cross-sectional study examined work impairment related to osteoarthritis (OA) among Japanese workers and reported greater medication use, lower health-related quality of life, and higher depression severity among patients with OA than among those without OA [5]. Furthermore, KOA has been reported to have greater societal costs and more associated disability than OA of any other joint [6].

In Japan, the prevalence of chronic musculoskeletal pain is greatest in the population of working individuals in their 30s to 50s, with the low back being the most commonly reported site of chronic pain [7]. Low back pain (LBP) impairs physical activities such as walking and standing and is estimated to affect 16.9% of men

and 20.0% of women in Japan [8]. Coexistence of LBP and knee pain and that of lumbar spondylosis and KOA were reported by 12.2% of Japanese community participants (n = 12,019) [9] and 34.8% of a large Japanese population cohort (n = 3,040) [4], respectively, in Japan. LBP is a common comorbidity associated with KOA, occurring in more than 55% of patients with KOA and often intensifying their knee pain and disability [10, 11]. Recently conducted meta-analyses reported LBP to be a significant predictor of KOA symptoms and related disability [12, 13]. The prevalence of pain can increase dramatically for patients with KOA with concomitant back problems compared with patients with only KOA [14]. Furthermore, LBP intensifies both knee pain and disability level for individuals with KOA [13].

Currently, no definitive treatment options exist for either KOA or LBP, and the severity of each condition differs across individual patients, especially in case of KOA combined with LBP. Current options for managing pain related to KOA or LBP may include pharmacological and nonpharmacological modalities, alone or in combination [15, 16]. Whereas physical therapy and pharmacological pain relief (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs]) may relieve pain symptoms and improve knee function, they do so only temporarily and to a limited degree [17]. Early diagnosis and treatment of early-stage KOA at a younger age become critical to delay progression to highly degenerative KOA [18]. Although surgical treatment (e.g., total knee arthroplasty) may significantly decrease pain symptoms and improve range of motion for patients with KOA, it is recommended only for advanced KOA or when conservative treatment is ineffective [17, 19]. Pain management options for early-stage KOA are limited [20], and there is a lack of information on pain management patterns for combined KOA and LBP, which often occurs in the working-age population.

To address the knowledge gap, we conducted a retrospective database study, the primary objectives of which were to assess the long-term comorbidity burden and medical resource utilization among working-age patients with KOA with and without LBP in Japan. The secondary objective was to document long-term direct medical costs among patients with KOA with or without LBP in Japan.

Methods

Data Source
Data for this retrospective cohort study were derived from de-identified health insurance claims filed between January 1, 2010, and December 31, 2017, in the Japan Medical Data Center (JMDC) database [21]. The database includes information predominantly of persons of working age (i.e., <65 years old), employed by middle-to large-sized companies, as well as their dependents. At the time the study was conducted, the database included >3 million unique persons from 2003 onward and represented approximately 2.5% of the total population of Japan.

Patient Selection and Study Cohorts
The study population was selected from patients more than 40 years of age with an *International Classification of* Diseases, *Tenth Revision, Clinical Modification* (ICD-10-CM) diagnosis of KOA (ICD-10-CM code M17) that was documented between January 1, 2011, and December 31, 2012. The date of first KOA diagnosis between January 1, 2011, and December 31, 2012, defined the index date (Figure 1). Patients were excluded from the study if they had at least one diagnosis of OA with ICD-10 code M16 (hip), M18 (first carpometacarpal joint), or M19 (other and unspecified) at any point of study period or diagnosis of malignancy (ICD-10 codes C00–C97 and D00–D09) during the follow-up period. All patients were required to have a minimum of 1 year of enrollment before the index date (i.e., baseline period) and 5 years of enrollment after the index date (i.e., follow-up period). To ascertain the diagnosis, patients were further required to have at least one additional KOA diagnosis at any point during the 5-year follow-up period and no diagnoses for KOA during the baseline period. Patients with a diagnosis of malignancy during the 5-year follow-up period were excluded from the study to avoid the potential for the significant health care resources and costs associated with cancer treatment for these individuals to skew the health care resource use (HCRU) and cost estimates.

This study included a cohort of patients with KOA only without LBP (KOA-noLBP) and a cohort of patients with KOA plus LBP (KOA+LBP). Definitions for these cohorts are as follows:

- **KOA+LBP cohort:** Patients were included in this cohort if they had at least one diagnosis of LBP in the baseline period or in the first 12 months after the index date (inclusive of the index date). ICD-10-CM codes for LBP are presented in the Supplementary Data.
- **KOA-noLBP cohort:** Patients were included in this cohort if they did not have any diagnosis of LBP (ICD-10-CM codes M40, M41, M43, M47, M48, M51, M53, and M54) in the baseline and follow-up periods.

Because the patient data used in this study were anonymized, the Ethical Guidelines for Medical and Health Research Involving Human Subjects (Ministry of Education, Culture, Sports, Science and Technology and Ministry of Health, Labour and Welfare of Japan) were not applicable to this study. This study was reviewed by RTI International's Institutional Review Board and was granted a waiver from full review as the data were de-identified, retrospective, and collected for billing purposes.
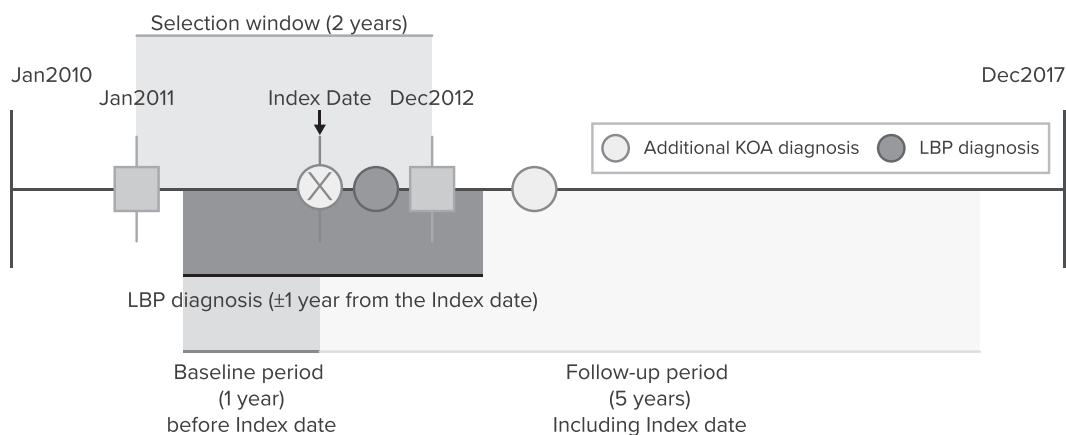
Figure 1. Study scheme.

Study Measures and Definitions

The study evaluated patient demographics, clinical characteristics, pain management patterns, HCRU, and direct medical costs. Demographic characteristics measured at the index date included age and sex. The distribution of treating physicians' specialty (i.e., orthopedic surgeons, rheumatologists, anesthesiologists, internal medicine/general practitioners) and the type of institution (i.e., public hospital, university hospital, clinic) for the KOA diagnosis on the index date were reported. Long-term comorbidities, which the Osteoarthritis Research Society International has recommended considering in the treatment of OA [22], as described in the Supplementary Data, were examined during both the baseline period and in each year of the 5-year follow-up period.

Longitudinal pain management patterns were assessed. The number and percentage of patients with broad categories of treatment (i.e., nonpharmacological treatment, pharmaceutical treatment, injectable treatment, and surgery) during each year of the 5-year follow-up period were evaluated. Nonpharmacological treatments included physical therapy and manual/instrumental therapy, such as thermotherapy, massage, infrared therapy, electric therapy, compression therapy, and ultrasound therapy. Pharmaceutical and injectable (i.e., corticosteroids, intra-articular hyaluronic acid, and trigger point injection) treatments were identified on the basis of product generic and brand names, as well as therapeutic class descriptions as recorded in the study database. Medical procedures were identified on the basis of unique Japanese procedure codes.

For each patient, OA-related HCRU and costs were documented. OA-related hospital admissions were identified by searching for inpatient hospital confinements in which OA or LBP was recorded as the primary discharge diagnosis or in which an OA procedure occurred (i.e., arthroscopic surgery, osteotomy, arthroplasty, arthrodesis). OA-related outpatient visits were identified by searching for medical claims with any diagnosis (i.e., primary or secondary) of OA or LBP, an OA or LBP procedure, a

nonpharmacological treatment modality, or administration of injectable treatments.

All-cause and OA-related HCRU and costs were estimated during each year of the 5-year follow-up period. Detailed information on OA-related visits were reported by stratifying cost measures by the service type (i.e., OA-related inpatient surgeries, outpatient surgeries, outpatient visits for imaging, outpatient visits for nonpharmacological treatment, outpatient visits for injections, and outpatient visits for medication) and time period (e.g., year 1 follow-up, year 2 follow-up). Specifically, the proportions of patients with an inpatient or outpatient visit were reported. Similarly, the mean number of outpatient visits during the relevant period was reported. The costs represented payments for medical services and prescription drugs. The costs associated with medical care received included the insurance payment and patient copayment amount. All cost data were reported in Japanese yen (¥) and were inflated to 2017 prices by using the medical care component of the Japanese Consumer Price Index [23].

Statistical Analysis

Patient demographics, clinical characteristics, pain management patterns, and all-cause and OA-related HCRU and costs were reported for the KOA-noLBP and KOA+LBP cohorts.

Descriptive analyses entailed the tabular display of mean values and standard deviations of continuous variables of interest (e.g., HCRU) and frequency distributions for categorical variables (e.g., sex). The statistical significance of descriptive differences in patient characteristics, pain management patterns, and health care resource use between the KOA-noLBP and KOA+LBP cohorts were tested with the Student t test, chi-squared test, and Fisher exact test, as appropriate, with results of significance reported. Bivariate descriptive statistics were used to calculate HCRU and costs in the KOA-noLBP and KOA+LBP cohorts. A critical value of 0.05 was used to determine statistical significance. All analyses were
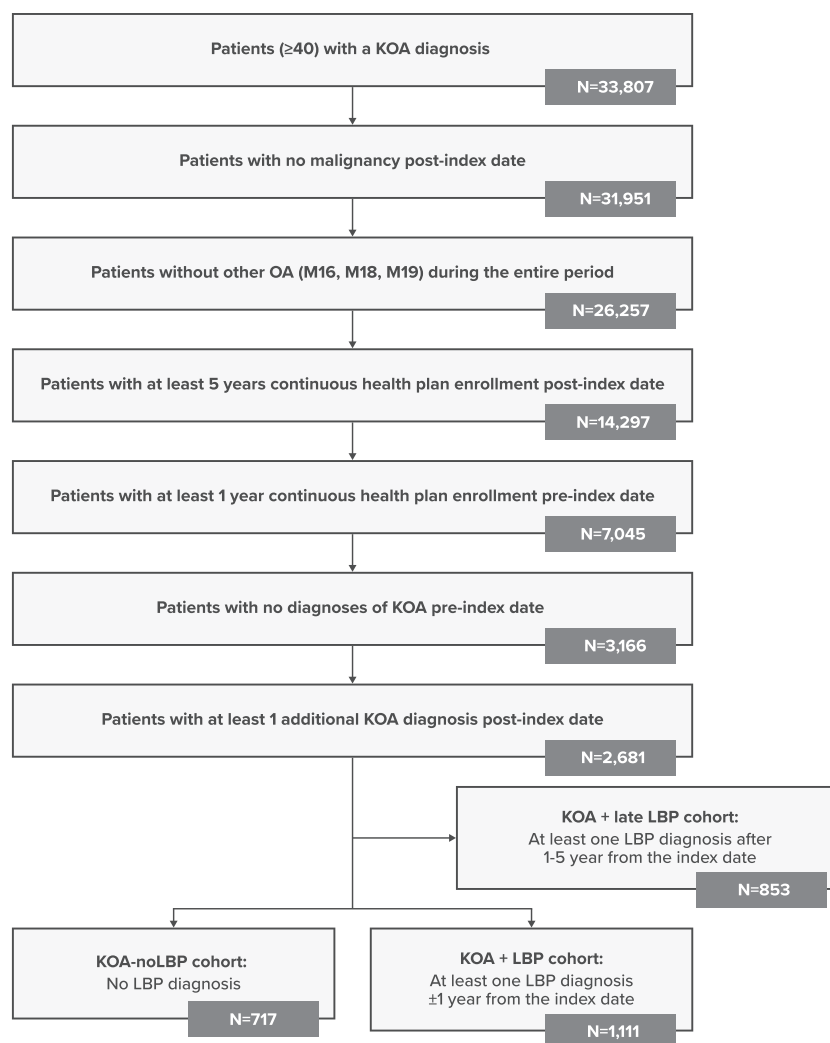
Figure 2. Selection flow. M16–M19 are ICM-10-CM codes.

conducted in SAS version 9.3 or later (SAS Institute, Inc., Cary, North Carolina, USA).

Results

Of the 2,681 patients who met the initial study criteria, 853 patients (31.8%) had at least one LBP diagnosis after the first year from the index date. A total of 1,828 patients met the final study criteria: 717 in the KOA-noLBP cohort and 1,111 in the KOA+LBP cohort (Figure 2). Patient demographics are presented in Table 1. Mean age was similar among the KOA+LBP (53.1 years) and the KOA-noLBP (52.1 years) cohorts, and more females were in the KOA+LBP cohort than in the KOA-noLBP cohort (55.0% vs. 49.4%). A higher proportion of patients were 60 years of age or older in the KOA+LBP cohort (19.3%) than in the KOA-noLBP cohort (13.5%). More than 80% of patients in both cohorts were 40–59 years of age, which highlights the disease burden among the younger working-age

population. Across both cohorts, most patients visited orthopedic surgery clinics on the index date.

A higher proportion of patients had at least one comorbidity to be considered for OA treatment in the KOA+LBP cohort (34.6%) than in the KOA-noLBP cohort (19.9%) (Table 1). The details of reported comorbidities during the baseline and 5-year follow-up periods are presented in Figure 3. During the baseline and follow-up periods, a higher percentage of patients in the KOA+LBP cohort had a diagnosis of diabetes, hypertension, cardiovascular disorders, and depression relative to the KOA-noLBP cohort.

The proportions of patients who received treatment for OA during each year of the 5-year follow-up period are presented in Figure 4 and Table 2. Nonpharmacological treatments were received by 40.3% of patients in the KOA+LBP cohort and by 22.2% in the KOA-noLBP cohort during the first year of the follow-up period. Regardless of cohort, manual/instrumental therapy was the most common nonpharmacological treatment received (Table 2). The proportion of patients

Table 1. Patient characteristics

Characteristic	KOA-noLBP (n = 717)	KOA+LBP (n = 1,111)
Age at index date, mean (SD) [min–max], y	52.1 (6.8) [40–71]	53.1 (7.2) [40–71]
Age categories, n (%), y		
40 to 49	279 (38.9)	364 (32.8)
50 to 59	341 (47.6)	533 (48.0)
60 to 69	89 (12.4)	**195 (17.6)**
70 to 74	8 (1.1)	19 (1.7)
Female, n (%)	354 (49.4)	**611 (55.0)**
At least one comorbidity, n (%)	143 (19.9)	384 (34.6)
Physician department for index KOA diagnosis, n (%)		
Orthopedic surgery	554 (77.3)	849 (76.4)
Anesthesiology	4 (0.6)	4 (0.4)
Internal medicine internists	140 (19.5)	220 (19.8)
Other specialties	19 (2.7)	38 (3.4)
Type of site for the index KOA diagnosis, n (%)		
Public hospital	12 (1.7)	26 (2.3)
University hospital	5 (0.7)	12 (1.1)
Other hospital	101 (14.1)	150 (13.5)
Clinic	599 (83.5)	923 (83.1)

SD=standard deviation.

Bold values indicate $P < 0.05$.
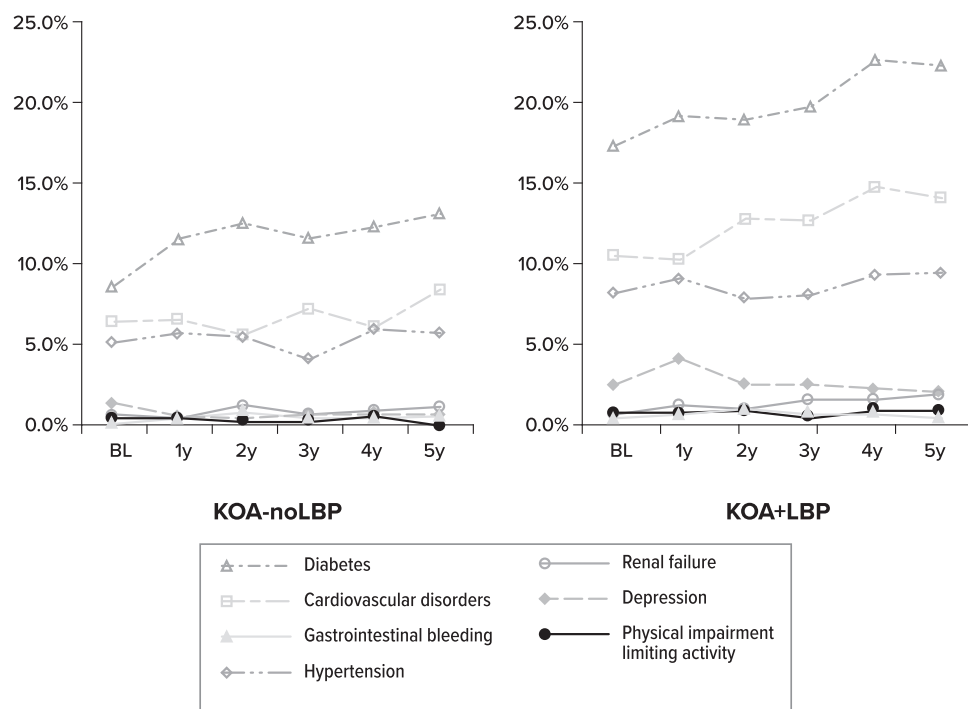
Figure 3. Proportion of comorbidities to consider for OA treatment, defined by Osteoarthritis Research Society International Guideline. BL = baseline.

receiving nonpharmacological treatments decreased in year 2 of the 5-year follow-up period and remained at approximately the same level for the remainder of the follow-up period (i.e., years 3 through 5).

Pharmaceutical treatment was received by 90.8% patients in the KOA+LBP cohort and 83.0% in the KOA-noLBP cohort during the first year of follow-up. The proportion of patients receiving pharmaceutical treatment decreased in the second year of follow-up and remained at approximately the same level for the remainder of the 5-year follow-up period (i.e., years 3 through 5). Regardless of the cohort, topical NSAIDs (received by 80.7% of patients in the KOA+LBP cohort and 71.7% of patients in the KOA-noLBP cohort), followed by oral NSAIDs and cyclooxygenase-2–selective inhibitors, were the most common pharmaceutical treatments received during the first year of the follow-up period. Weak opioids were received by 2.9% of patients in the KOA-
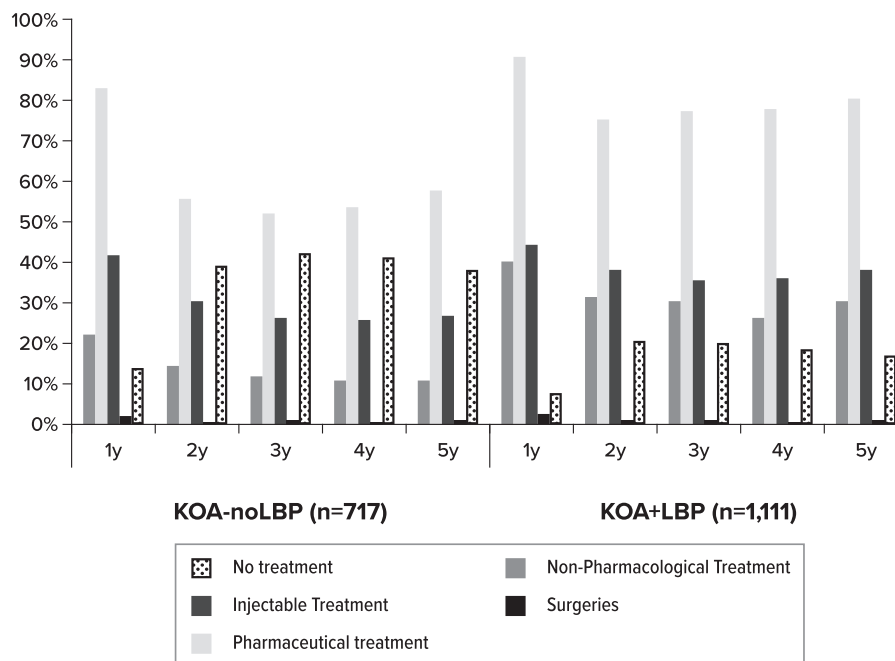
Figure 4. Proportion of treatment modality for each year of follow-up period.

Table 2. Treatment profiles observed each year

Treatment modality, %	KOA-noLBP ($n = 717$)					KOA+LBP ($n = 1,111$)				
	1 y	2 y	3 y	4 y	5 y	1 y	2 y	3 y	4 y	5 y
Nonpharmacological treatment										
Physical therapy	10.2	4.7	5.4	4.3	4.2	**18.7**	**14.3**	**14.3**	**11.9**	**14.5**
Manual/instrumental therapy	14.0	10.5	7.0	7.3	7.5	**26.9**	**20.9**	**20.6**	**18.4**	**20.0**
Pharmaceutical treatment										
NSAIDs, oral	51.9	35.0	32.1	34.7	34.2	**69.3**	**53.6**	**53.3**	**55.5**	**54.9**
NSAIDs, topical	71.7	33.6	29.0	28.9	34.5	**80.7**	**55.2**	**56.4**	**52.8**	**59.3**
COX-2–selective inhibitors	22.2	8.2	6.6	6.7	7.5	22.5	**12.2**	**10.7**	**10.4**	**12.2**
Acetaminophen	10.5	11.4	12.4	16.9	19.0	**18.3**	**19.9**	**21.0**	**25.5**	**28.7**
Weak opioid*	2.9	2.2	2.7	2.7	4.3	**6.2**	**6.7**	**6.7**	**7.0**	**7.8**
Strong opioid†	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.2	0.4
Other non-opioid drug	1.7	1.4	1.1	0.6	0.7	**9.1**	**6.6**	**6.4**	**6.1**	**6.6**
SNRI	0.4	0.6	0.6	0.3	0.6	**1.4**	**1.7**	**1.6**	**2.0**	**2.9**
Pregabalin	0.1	0.1	0.3	0.7	0.7	**5.0**	**4.5**	**6.2**	**4.8**	**6.8**
Injectable treatment										
Corticosteroids	23.3	16.5	16.3	16.5	17.6	**29.2**	**24.8**	**24.7**	**26.1**	**26.5**
Intra-articular hyaluronic acid	34.0	20.5	16.7	15.9	16.0	31.1	21.8	19.0	17.7	**20.1**
Trigger point injection	1.1	0.8	1.1	0.8	0.8	**6.5**	**6.7**	**6.5**	**5.9**	**6.6**

*Including codeine phosphate, dihydrocodeine phosphate, tramadol, and tramadol hydrochloride/acetaminophen.

†Including fentanyl, fentanyl citrate, oxycodone, buprenorphine, and morphine.

COX=cyclooxygenase; SNRI= serotonin-norepinephrine reuptake inhibitor.

Bold values indicate $P < 0.05$.

noLBP cohort and 6.2% of patients in the KOA+LBP cohort during the first year of the follow-up period, and these percentages did not tend to change over time. Strong opioids were rarely received across both the cohorts (Table 2).

Injectable treatment was received by 41.6% of patients in the KOA-noLBP cohort and 44.1% of patients in the KOA+LBP cohort; intra-articular hyaluronic acid and corticosteroids were the most common injectable treatments received during the first year of follow-up (Table 2). In total, 1.8% of patients in the KOA-noLBP cohort had surgery in the follow-up period vs. 2.3% of patients in the KOA+LBP cohort. Overall, about 40% of patients in the KOA-noLBP cohort and 20% in the KOA+LBP cohort did not receive any treatment between year 2 and year 5 of follow-up (Figure 4).

Analysis of the overall treatment regimens and order of therapies received by patients revealed that the most

Table 3. All-cause and OA-related health care resource use

Treatment modality	KOA-noLBP ($n = 717$)					KOA+LBP ($n = 1,111$)				
	1 y	2 y	3 y	4 y	5 y	1 y	2 y	3 y	4 y	5 y
Patients with services, %										
Outpatient visit										
OA related	100.0	37.5	30.5	29.4	30.5	99.9	**68.0**	**66.2**	**62.7**	**64.1**
All cause	100.0	89.4	87.6	88.7	91.1	99.9	96.4	96.7	96.8	97.0
Pharmacy visit										
OA related	69.0	41.3	38.2	40.2	39.5	**75.1**	**58.2**	**59.4**	**61.0**	**60.9**
All cause	82.0	70.9	68.2	72.1	71.8	89.8	82.8	84.4	85.4	86.1
Hospital admission										
OA related	0.7	0.4	0.3	0.3	0.7	**2.4**	0.6	0.6	**1.4**	**1.2**
All cause	2.2	2.0	2.1	1.1	2.9	4.1	2.6	3.3	3.3	3.7
Number of services, mean (SD)										
Outpatient visit										
OA related	3.8 (3.6)	1.8 (3.5)	1.6 (3.5)	1.5 (3.4)	1.6 (3.5)	**6.8 (5.2)**	**4.5 (5.4)**	**4.5 (5.5)**	**4.3 (5.5)**	**4.6 (5.8)**
All cause	9.3 (6.9)	7.5 (6.9)	7.5 (7.2)	7.7 (7.0)	8.0 (7.0)	14.9 (9.3)	13.0 (9.8)	13.0 (9.6)	13.0 (9.5)	13.7 (9.8)
Pharmacy visit										
OA related	3.4 (4.8)	1.7 (0.0)	1.7 (0.1)	1.6 (0.0)	1.6 (0.0)	**6.2 (8.9)**	**4.0 (0.1)**	**3.9 (0.1)**	**4.1 (0.1)**	**4.3 (0.1)**
All cause	9.4 (7.3)	7.3 (7.4)	7.3 (7.6)	7.3 (7.2)	7.7 (7.5)	15.0 (10.0)	12.8 (10.3)	12.8 (10.2)	12.9 (10.0)	13.6 (10.5)
Hospital admission										
OA related	0.0 (0.3)	0.0 (0.2)	0.0 (0.2)	0.0 (0.2)	0.0 (0.2)	0.0 (0.3)	0.0 (0.2)	0.0 (0.3)	0.0 (0.2)	0.0 (0.3)
All cause	0.0 (0.3)	0.0 (0.2)	0.0 (0.2)	0.0 (0.2)	0.0 (0.2)	0.1 (0.4)	0.0 (0.3)	0.0 (0.3)	0.0 (0.3)	0.1 (0.4)

Bold values indicate $P < 0.05$.
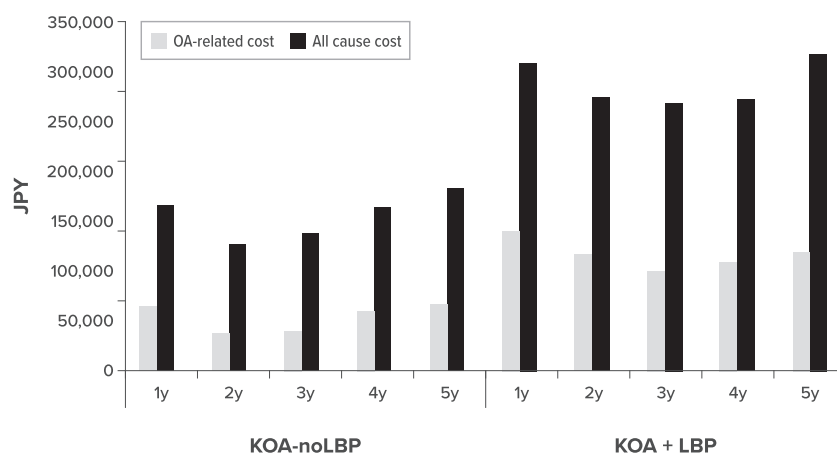
Figure 5. Total OA-related and all-cause cost.

common regimen first received was either topical or oral NSAIDs. A slightly higher mean number of pharmaceutical treatments were received by patients in the KOA+LBP cohort (3.6) relative to the KOA-noLBP cohort (2.7) during the follow-up period (data not shown).

Proportions of OA-related and all-cause resource use are presented in Table 3. Regardless of cohort, the percentage of patients with an OA-related hospitalization was low (~1% for KOA-noLBP and ~2% for KOA+LBP) during the entire follow-up period. Additionally, during each year of the 5-year follow-up period, higher mean numbers of OA-related outpatient visits were observed among patients in the KOA+LBP cohort (6.8, 4.5, 4.5, 4.3, and 4.6) than in the KOA-noLBP cohort (3.8, 1.8, 1.6, 1.5, and 1.6). Figure 5 and

the Supplementary Data present data on the total direct medical mean cost for both OA-related and all-cause health care resource costs. Both OA-related and all-cause costs were highest in the first year of follow-up and were observed to decrease in second year, but they gradually increased during the 3- to 5-year follow-up period. Total OA-related direct medical mean costs were higher among patients in the KOA+LBP cohort (¥140,472, ¥116,930, ¥100,292, ¥109,554, and ¥118,718) than in the KOA-noLBP cohort (¥64,003, ¥37,778, ¥40,114, ¥60,232, and ¥66,738) during each year of the 5-year follow-up period. Similar trends were observed for total all-cause direct medical mean costs across the two cohorts. Regardless of the cohort, more than 70% of total OA-related direct medical costs were attributed to OA-related medications (Supplementary Data).

Discussion

This study is one of the first to longitudinally assess pain management patterns along with health care resource use and direct medical costs for patients in Japan with KOA and LBP in a working population. Our research suggests that more than 73% of patients with KOA also had comorbid LBP during the study period. Previous studies have also reported a high proportion (70% to 90%) of patients with KOA with comorbid LBP, even in younger populations [10, 11]. In our study, a majority of patients in both cohorts received pharmaceutical treatment during the first year of follow-up. The proportion of patients in our study receiving pharmaceutical treatment decreased between the first year of follow-up and the second year of follow-up and remained stable at this level for the remainder of the follow-up period (i.e., year 3 through year 5). Topical and oral NSAIDs were the most frequently observed treatments received for pain management across both cohorts. Overall, patients with comorbid KOA and LBP (the KOA+LBP cohort) had a greater comorbidity burden and increased HCRU and costs relative to patients with KOA-noLBP. This study observed that the direct medical cost burden was highest during first year of the 5-year follow-up period, regardless of the cohort.

Patients with KOA, specifically KOA+LBP, were observed to have more comorbidities requiring consideration for conservative treatment of OA as recommended by Osteoarthritis Research Society International guidelines during both the baseline and follow-up periods. Diabetes, hypertension, cardiovascular disorders, and depression were observed in higher proportions of patients with KOA+LBP than those with KOA-noLBP during the baseline and 5-year follow-up periods. A meta-analysis of observational studies reported a higher proportion of comorbidities among patients with KOA [12]. A cross-sectional study also reported significant comorbid burden among all patients with OA of the knee or hip [24]. Another study assessing associations between patient comorbidity and use of treatment for KOA reported that those with comorbidity were 40% less likely to exercise than those without comorbidity [25]. Higher comorbidities in the KOA+LBP cohort than in the KOA-noLBP cohort in the present study also may have resulted in more frequent use of nonpharmaceutical treatments in this population, given the higher risks involved in using pharmaceutical treatments due to comorbidities.

Pain management patterns reported in our study may be compared with those from other retrospective observational studies. Akazawa and colleagues [26] reported treatment patterns of OA or chronic LBP using a Japanese hospital–based claims database. They reported similar treatment patterns, and NSAIDs were the most prescribed class of analgesics for the management of OA and chronic LBP regardless of a different target population and the use of a hospital-based database. However,

the results of their study may not be directly comparable to our study given the chronic nature of the LBP diagnosis assessed in their study vs. the assessment of all LBP in the present analysis. Other studies conducted in the United States and United Kingdom have also reported pain management patterns among patients with chronic LBP over a 12-month follow-up period; however, no study has assessed longitudinal pain management patterns in an overall LBP cohort, as was done in our analysis [27–29].

Overall, higher HCRU and costs were observed among patients with KOA+LBP than among patients with KOA-noLBP during the 5-year follow-up period. Furthermore, the present study reported the highest OA-related medical costs in the first year after the index KOA diagnosis, which could be explained by the more frequent diagnostic and outpatient care visits during the initial year of OA diagnosis. Similarly, Le et al. [30] conducted a retrospective analysis and reported that patients with a new diagnosis of OA incurred higher medical costs than those of existing patients. Specifically, Le et al. [30] reported mean total all-cause costs of US $19,391 and OA-related costs of US $6,811 among newly diagnosed OA patients. Another study conducted in Singapore reported annual direct costs ranging from 1,460 to 7,477 Singaporean dollars among patients with KOA [31]. However, few studies conducted in other countries have reported medical costs among patients with KOA or LBP. To our knowledge, the present study is the first study to longitudinally report the cost burden related to KOA with or without LBP in Japan.

There are some limitations to be noted in our study. First, the study sample was selected from enrollees covered by the employees' health insurance system. Because most enrollees are working adults or the family members of working adults, the proportion of elderly patients 65 years of age or older is low. The present study may overestimate OA-related costs by incorporating costs attributed to OA-comorbidity–related pharmacy use (e.g., serotonin-norepinephrine reuptake inhibitor treatment for depression). Although surgical claims codes were collected to identify arthroscopic surgery, osteotomy, artificial joint replacement, and joint fusion, the surgical sites for these procedures could not be identified. Finally, because the diagnoses listed in the claims were not validated, it was not possible to confirm patient diagnoses, potentially compromising the all-cause vs. OA-related HCRU analysis.

In Japan, arthralgia is one of the most frequently encountered symptoms among the elderly population, which constitutes a growing segment of Japanese demographics; furthermore, comorbid chronic diseases and disability in the elderly have become a major public health concern from a socioeconomic perspective [32]. The present study highlights a need for research focused not only on treatments solely for KOA pain but also on multidisciplinary and comprehensive treatments

specifically for KOA with comorbid LBP, including other associated comorbidities from internal medicine points of view, in Japan. Clinicians should consider focusing on treatments that would benefit LBP along with KOA, given the extent of the disease and the greater health care burden observed in this comorbid population. According to clinical guidelines, multidisciplinary treatments recommended for the treatment of KOA, such as exercise and manual therapy, weight loss, acupuncture, thermotherapy, analgesics, intra-articular injections, and surgeries, may also benefit patients with KOA and LBP.

Conclusion

This study is the first to demonstrate that patients with KOA and LBP received a greater proportion of pain-related treatment relative to patients with KOA only. The results of the present analysis suggest that multidisciplinary and comprehensive treatment for not only KOA but also LBP may be important for effective resource use in an aging society coping with socioeconomic burdens.

Acknowledgments

Supplementary Data

Supplementary Data may be found online at http://pain-medicine.oxfordjournals.org.

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