Title
Knee Osteoarthritis Treatment Costs in the Medicare Patient Population.

Journal
American Health & Drug Benefits, 13(4)

ISSN
1942-2962

Authors
Malanga, Gerard
Niazi, Faizan
Kidd, Vasco Deon
et al.

Publication Date
2020-09-01

ORIGINAL RESEARCH

Knee Osteoarthritis Treatment Costs in the Medicare Patient Population

Gerard Malanga, MD; Faizan Niazi, PharmD; Vasco Deon Kidd, DHSc, MPH, MS, PA-C; Edmund Lau, MS; Steven M. Kurtz, PhD; Kevin L. Ong, PhD, PE; Andrew L. Concoff, MD, FACR, CAQSM

BACKGROUND: Several nonoperative options have been recommended for the treatment of knee osteoarthritis (OA), with varying degrees of evidence. Adhering to the American Academy of Orthopaedic Surgeons clinical practice guidelines has been suggested to decrease direct treatment costs by 45% in the year before knee arthroplasty, but this does not consider the cost of the entire episode of care, including the cost of surgery and postsurgery care.

OBJECTIVES: To analyze the total treatment costs after a diagnosis of knee OA, as well as the proportion of arthroplasty interventions as part of the total knee OA–related costs, and whether the total costs differed for patients who received intra-articular hyaluronic acid and/or had knee arthroplasty.

METHODS: We identified patients newly diagnosed with knee OA using the 5% Medicare data sample from January 2010 to December 2015. Patients were excluded if they were aged <65 years, had incomplete claim history, did not reside in any of the 50 states, had claim history <12 months before knee OA diagnosis, or did not enroll in Medicare Part A and Part B. The study analyzed knee OA–related costs from a payer perspective in terms of reimbursements provided by Medicare, as well as the time from the diagnosis of knee OA to knee arthroplasty for patients who had knee arthroplasty, and the time from the first hyaluronic acid injection to knee arthroplasty for those who received the injection. We compared patients who received hyaluronic acid and those who did not receive hyaluronic acid injections. Patients who received hyaluronic acid injection who subsequently had knee arthroplasty were also compared with those who did not have subsequent knee arthroplasty.

RESULTS: Of the 275,256 patients with knee OA, 45,801 (16.6%) received a hyaluronic acid injection and 35,465 (12.9%) had knee arthroplasty during the study period. The median time to knee arthroplasty was 16.4 months for patients who received hyaluronic acid versus 5.7 months for those who did not receive hyaluronic acid. Non–arthroplasty-related therapies and knee arthroplasty accounted for similar proportions of knee OA–related costs, with hyaluronic acid injection comprising 5.6% of the total knee OA–related costs. For patients who received hyaluronic acid injections and subsequently had knee arthroplasty, hyaluronic acid injection contributed 1.8% of the knee OA–related costs versus 76.6% of the cost from knee arthroplasty. Patients who received hyaluronic acid injections and did not have knee arthroplasty incurred less than 10% of the knee OA–related costs that patients who had surgery incurred.

CONCLUSION: Although limiting hyaluronic acid use may reduce the knee OA–related costs, in this study hyaluronic acid injection only comprised a small fraction of the overall costs related to knee OA. Among patients who had knee arthroplasty, those who received treatment with hyaluronic acid had surgery delayed by a median of 10.7 months and associated costs for a significant period. The ability to delay or avoid knee arthroplasty altogether can have a substantial impact on healthcare costs.

Am Health Drug Benefits. 2020;13(4):144-153
www.AHDBonline.com

Manuscript received November 11, 2019
Accepted in final form March 31, 2020

Disclosures are at end of text
Supplemental material online

KEY WORDS: direct costs, healthcare costs, hyaluronic acid injection, knee arthroplasty, knee osteoarthritis, Medicare patients

Knee osteoarthritis (OA) places a substantial health burden on patients, and also places an economic burden on the healthcare system. Knee OA contributes to more than $27 billion in annual healthcare costs, with expenditures related to total knee arthroplasty exceeding $11 billion annually.[1-3] In addi-

Dr Malanga is Clinical Professor, Department of Physical Medicine and Rehabilitation, Rutgers School of Medicine–NJ Medical School, Newark, NJ, and Founder/Partner, New Jersey Regenerative Institute, Cedar Knolls; Dr Niazi is Medical Director, Medical Affairs, Specialty Products, Ferring Pharmaceuticals, Parsippany, NJ; Dr Kidd is Director of Advanced Practice Providers, Office of Advanced Practice and Department of Orthopedic Surgery, University of California Irvine, UCI Health, Orange; Mr Lau is Senior Managing Scientist, Exponent, Menlo Park, CA; Dr Kurtz is Practice Director and Principal, and Dr Ong is Principal Engineer, Exponent, Philadelphia, PA; Dr Concoff is Chief Value Medical Officer, United Rheumatology, Hauppauge, NY.

KEY POINTS

- Knee osteoarthritis (OA) is associated with a significant health burden on patients and an economic burden on the healthcare system.
- This analysis of Medicare patients compared the overall knee OA treatment costs for patients who received intra-articular hyaluronic acid injection versus knee arthroplasty.
- Of 275,256 patients newly diagnosed with knee OA, 16.6% received a hyaluronic acid injection and 12.9% had knee arthroplasty.
- Among those who received hyaluronic acid and had arthroplasty, hyaluronic acid use delayed surgical intervention by 15 months.
- The median time to knee arthroplasty was 10.7 months longer with hyaluronic acid versus no use of hyaluronic acid (16.4 months vs 5.7 months).
- For patients who received hyaluronic acid and had knee arthroplasty, hyaluronic acid treatment contributed 1.8% of the costs versus 76.6% of the cost from arthroplasty.
- Hyaluronic acid injections can delay or reduce the need for knee arthroplasty and lower the costs for knee OA, thereby potentially affecting the total healthcare costs.

tion to total knee arthroplasty, several nonsurgical therapies are frequently considered for the treatment of patients with knee OA. The 2013 American Academy of Orthopaedic Surgeons (AAOS) clinical practice guidelines recommend physical therapy, nonsteroidal anti-inflammatory drugs (NSAIDs), and tramadol for the treatment of knee OA, but these guidelines are either inconclusive about the use of corticosteroid, opioids, and knee braces or recommend against the use of hyaluronic acid injections.[4]

Bedard and colleagues have estimated that the treatment costs before knee arthroplasty could be reduced by up to 45% if only therapies recommended by the AAOS guidelines were used.[5] However, the previous study, as well as Cohen and colleagues, focused on expenditures leading up to knee arthroplasty, but not the entire episode of care, inclusive of the costs from the knee arthroplasty surgery itself or any post–knee arthroplasty care.[5,6] Furthermore, presurgical therapies only account for a small portion of the direct knee OA–related medical costs. For example, it has been estimated that intra-articular steroid injections have costs comparable to those for occasional analgesics but substantially less than the costs for total knee arthroplasty.[7]

With increasing utilization and costs of arthroplasty,[8,9] therapies that allow patients to avoid surgery may help to reduce the overall healthcare costs. Intra-articular hyaluronic acid is a nonsurgical option that reduces pain, improves functionality, and may aid in delaying the time to knee arthroplasty.[10-14] The additional time to knee arthroplasty may further help patients wean off of opioid treatment[15-17] or address modifiable patient risk factors,[18-20] which, in turn, can have a favorable impact on the knee arthroplasty outcomes. If access to nonsurgical interventions is reduced, it may lead to earlier use of the more costly knee arthroplasty,[21] including the associated follow-up care and the risk for a revised knee arthroplasty.

To address the limitations of available studies that have focused on the presurgical costs and did not compare surgical and nonsurgical interventions, the present study evaluated whether arthroplasty interventions would account for the majority of knee OA–related costs in the Medicare patient population. In addition, we compared the costs of knee OA–related care for Medicare patients who received hyaluronic acid injection and/or had knee arthroplasty with the costs for those who did not have one or both therapies.

Methods

Newly diagnosed patients with knee OA were identified from the 5% systematic sample of Medicare beneficiaries and their corresponding claims data (hospital inpatient, hospital outpatient, and Part B [physician/carrier] files) from January 1, 2010, to December 31, 2015. Of note, at the time of the initiation of this study, data from 2015 were the most recent Medicare data available.

The 5% data set is compiled by the Centers for Medicare & Medicaid Services (CMS) based on a random sample from selecting beneficiaries who had the same last 2 digits of their Health Insurance Claim number. Because the same set of beneficiary identification numbers is used from year to year, this data set allows for the same patients to be tracked longitudinally over time, with essentially 100% follow-up, unless patients move outside of the United States or die.

We accessed the database in the Medicare limited data set format, representing the fee-for-service claims submitted by healthcare providers to CMS. This limited data set contains beneficiary level–protected health information, but the selected variables are encrypted, blanked, or ranged. Although the limited data set is available as a 5% or 100% sample (5% or 100% of the beneficiaries), the 100% sample was not used in our study because, unlike the 5% data, the 100% data lacked physician or carrier and durable medical equipment claims.

Patients diagnosed with knee OA were identified based on the *International Classification of Diseases, Ninth*

Table 1 Study Demographic Characteristics

Characteristics		Patients with knee OA, N (%)	Patients with knee arthroplasty, N (%)	Patients receiving hyaluronic acid, N (%)
Sex	Age, yrs			
Male	65-69	30,880 (31.1)	5181 (37.1)	5414 (32.8)
	70-74	24,815 (25)	4155 (29.7)	4293 (26)
	75-79	19,071 (19.2)	2868 (20.5)	3244 (19.7)
	80-84	13,742 (13.8)	1360 (9.7)	2172 (13.2)
	≥85	10,832 (10.9)	405 (2.9)	1374 (8.3)
	Total	99,340 (100)	13,969 (100)	16,497 (100)
Female	65-69	49,725 (28.3)	7951 (37)	9604 (32.8)
	70-74	39,925 (22.7)	6253 (29.1)	7380 (25.2)
	75-79	32,874 (18.7)	4399 (20.5)	5570 (19)
	80-84	26,514 (15.1)	2255 (10.5)	3957 (13.5)
	≥85	26,878 (15.3)	638 (3)	2793 (9.5)
	Total	175,916 (100)	21,496 (100)	29,304 (100)
Census region				
Midwest		66,077 (24)	9821 (27.7)	10,172 (22.2)
North East		52,618 (19.1)	5327 (15)	9528 (20.8)
South		109,540 (39.8)	13,941 (39.3)	18,053 (39.4)
West		47,021 (17.1)	6376 (18)	8048 (17.6)
Total		275,256 (100)	35,465 (100)	45,801 (100)
Charlson Comorbidity Index score				
0		89,021 (32.3)	14,940 (42.1)	16,128 (35.2)
1-2		104,935 (38.1)	13,765 (38.8)	17,952 (39.2)
3-4		50,183 (18.2)	4902 (13.8)	7727 (16.9)
≥5		31,117 (11.3)	1858 (5.2)	3994 (8.7)
Total		275,256 (100)	35,465 (100)	45,801 (100)

OA indicates osteoarthritis.

Revision (*ICD-9*) and *ICD-10* codes for knee OA (see **Supplemental Table 1**, at **www.AHDBonline.com**). To limit the study inclusion to patients who were newly diagnosed with knee OA, we required that patients had at least a 12-month period of data before their study enrollment with a first knee OA diagnosis.

For patients with knee OA in 2010, the 2009 CMS data were used to evaluate whether the diagnosis was new. The exclusion criteria included patients aged <65 years, because they qualified for Medicare coverage through physical disability, had amyotrophic lateral sclerosis, or had end-stage renal disease, which might have skewed the findings. Patients who had an incomplete claim history (eg, those enrolled in a health maintenance organization [HMO]), did not reside in 1 of the 50 US states, had a claim history from less than 12 months before being diagnosed with knee OA, or who were not enrolled in Medicare Parts A and B, were also excluded from the study. In addition, patients with HMO coverage were excluded, because managed care organizations do not submit all claims for healthcare utilization to CMS; hence, claims for those patients in the CMS data set would be incomplete.

Patients who received hyaluronic acid injections and/or had knee arthroplasty were identified from this knee OA cohort using corresponding procedure codes (**Supplemental Table 2**, at **www.AHDBonline.com**). The knee OA–related direct costs, including Medicare reimbursements for medical services with a knee OA diagnosis, were compiled from all prescription medications. All costs were adjusted to 2017 dollars.

The knee OA–related claims (ie, claims with a knee OA diagnosis) were compiled for the patients from the time of their diagnosis of knee OA until the end of 2015. For patients with the longest follow-up (ie, those who were diagnosed with knee OA in 2010), the median cumulative knee OA–related costs were determined on a monthly basis 4 years after the knee OA diagnosis.

For all patients with knee OA, the overall knee OA–related costs were determined based on all costs associated with a knee OA diagnosis. Specific cost categories also included costs for hyaluronic acid, primary knee arthroplasty, revision knee arthroplasty (ie, repair of the first arthroplasty), physical therapy, intra-articular corticosteroids, arthrocentesis, knee arthroscopy, knee braces, anesthesia for knee surgery, ultrasound/fluoroscopic imaging, knee imaging (not including ultrasound or fluoroscopic imaging), and outpatient office visits (Supplemental Table 2).

Office visits were identified as claims with an outpatient office as the site of service. Because arthrocentesis and outpatient office visits may be for hyaluronic acid or for corticosteroid injections, the knee OA–related costs for outpatient visits were further stratified by the costs coded with a hyaluronic acid injection, with a corticosteroid injection, or without hyaluronic acid or corticosteroid injections. The knee OA–related costs were stratified for patients with and without knee arthroplasty and for those with and without hyaluronic acid injections.

The time from knee OA to surgery was also evaluated for all patients who had knee arthroplasty (total knee arthroplasty or unicondylar knee arthroplasty), as well as the time from the first hyaluronic acid injection to knee arthroplasty for the subset of patients who also received hyaluronic acid injections.

Results

Of the 275,256 patients with knee OA who met the inclusion criteria, 45,801 (16.6%) received a hyaluronic acid injection and 35,465 (12.9%) had knee arthroplasty during the study period (**Table 1**).

Of the patients with knee OA who were diagnosed in

2010 (ie, who had the longest follow-up), those who received hyaluronic acid injections had a cumulative knee OA–related treatment cost spike approximately 15 months later than the patients who did not have hyaluronic acid use (**Figure 1**).

A total of 1942 (30%) of the 6473 patients with knee OA who were diagnosed in 2010 and received hyaluronic acid injections eventually had knee arthroplasty within the study period after receiving the injection. The patients who had undergone knee arthroplasty incurred a median knee OA–related cost of $19,911 over the 4-year period (**Figure 2**), which is approximately 11 times more than the cost for the patients who received hyaluronic acid injections and did not have knee arthroplasty ($1839).

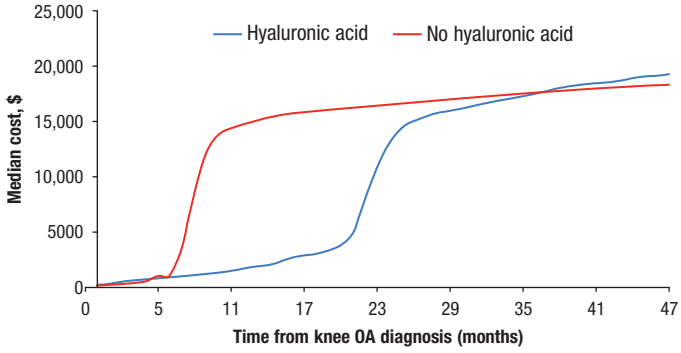
The overall knee OA–related costs totaled $1.196 billion for the 275,256 patients with knee OA (mean, $4347) over the study period. The mean knee OA–related cost per patient was $21,675 in the cohort that had knee arthroplasty compared with $1677 in the cohort that did not have knee arthroplasty. For the hyaluronic acid group, the mean knee OA–related cost was $23,393 if the patient had knee arthroplasty and $3398 if the patient did not have knee arthroplasty. The mean knee OA–related cost for the group that did not have hyaluronic acid injection was $20,940 if the patient had knee arthroplasty and $1383 if the patient did not have knee arthroplasty. Knee arthroplasty accounted for 51% of the overall knee OA–related costs in the knee OA cohort (**Figure 3**) but contributed to 76.6% of the knee OA–related costs when limited to the knee arthroplasty cohort.

Office visits accounted for 14.6% of the overall knee OA–related costs, whereas arthrocentesis, hyaluronic acid, knee imaging, physical therapy, and corticosteroid injections contributed 8.7%, 5.6%, 4%, 3.8%, and 3.6% of the costs, respectively. Of the knee OA–related office visit costs, 37% included hyaluronic acid (already in hyaluronic acid category) and 20.7% included corticosteroid (already in the corticosteroid category), whereas 44.5% did not include hyaluronic acid or corticosteroid injections.

Of the knee OA–related arthrocentesis costs, 59.5% included hyaluronic acid (already in the hyaluronic acid category) and 36.1% included corticosteroid injections (already in the corticosteroid category), whereas 8.3% did not include hyaluronic acid or corticosteroid injections.

When stratified by the time period before knee arthroplasty, office visits, arthrocentesis, hyaluronic acid, and knee imaging accounted for 28.9%, 18.8%, 12.1%, and 9.9% of the knee OA–related costs, respectively, in the 12 months before having knee arthroplasty (**Figure 4**). Of the knee OA–related office visit costs, 39.9% included hyaluronic acid (already in the hyaluronic acid category) and 21.5% included corticosteroid injections (already in the corticosteroid category), whereas 40.8% did not include hyaluronic acid or corticosteroid injections. Of the knee OA–related arthrocentesis costs, 61.2% included hyaluronic acid (already in the hyaluronic acid category) and 35.8% included corticosteroids (already in the corti-

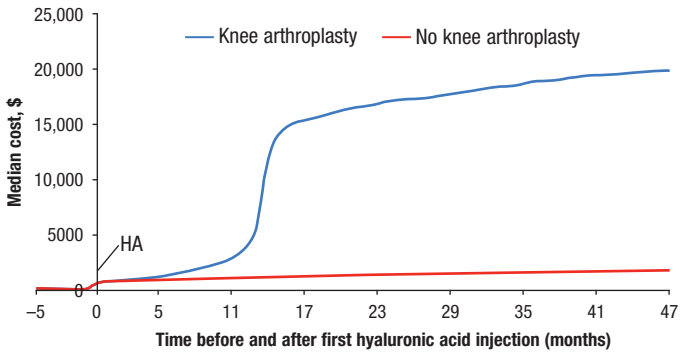
Figure 1 Median Cumulative Cost of Knee OA from Diagnosis and Hyaluronic Acid Use in Patients with Knee Arthroplasty[a]



Time, mo	0	5	11	17	23	29	35	41	47
Patients received HA, N	3716	3713	3707	3695	3689	3676	3656	3627	3598
Patients did not receive HA, N	7762	7748	7720	7680	7630	7567	7491	7423	7338

[a]Based on patients who were diagnosed with knee OA in 2010.
HA indicates hyaluronic acid; OA, osteoarthritis.

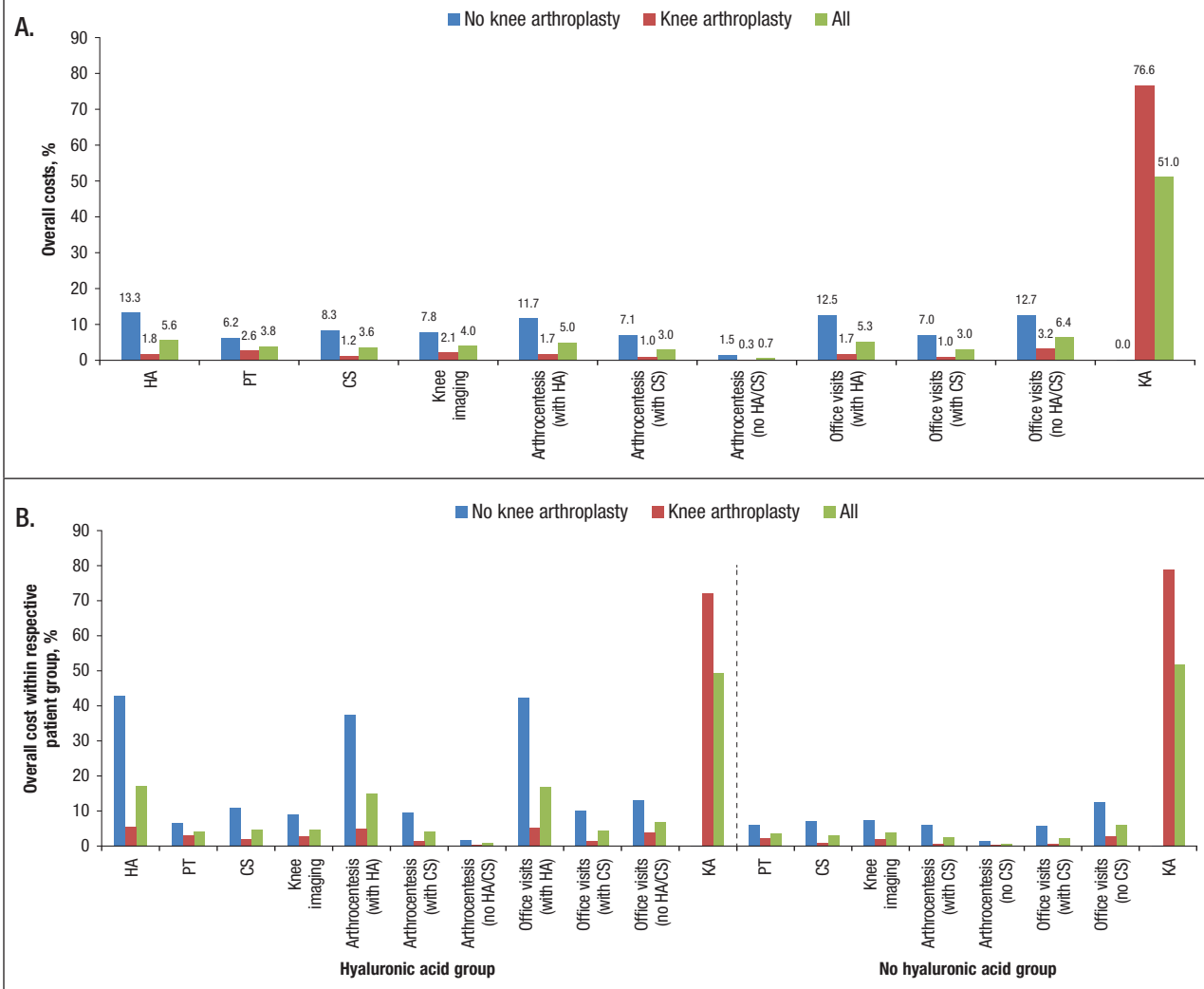
Figure 2 Median Cumulative Cost of Knee OA Before and After Hyaluronic Acid Injection for Patients with/without Knee Arthroplasty[a]



Time, mo	–5	0	5	11	17	23	29	35	41	47
Patients received HA & had KA, N	208	1942	1939	1933	1925	1920	1911	1895	1880	1856
Patients received HA but no KA, N	417	4531	4505	4421	4325	4227	4129	4019	3895	3804

[a]Based on patients who were diagnosed with knee OA in 2010.
HA indicates hyaluronic acid; KA, knee arthroplasty; OA, osteoarthritis.

Figure 3 Overall Knee OA–Related Costs (A) with and without Knee Arthroplasty, (B) Stratified by Previous Hyaluronic Acid Use[a]



[a]Arthrocentesis and office visits with hyaluronic acid or corticosteroid have been included in the hyaluronic acid and corticosteroid categories.
CS indicates corticosteroid injections; HA, hyaluronic acid; KA, knee arthroplasty; OA, osteoarthritis; PT, physical therapy.

costeroid category), whereas 6.6% did not include hyaluronic acid or corticosteroid injections.

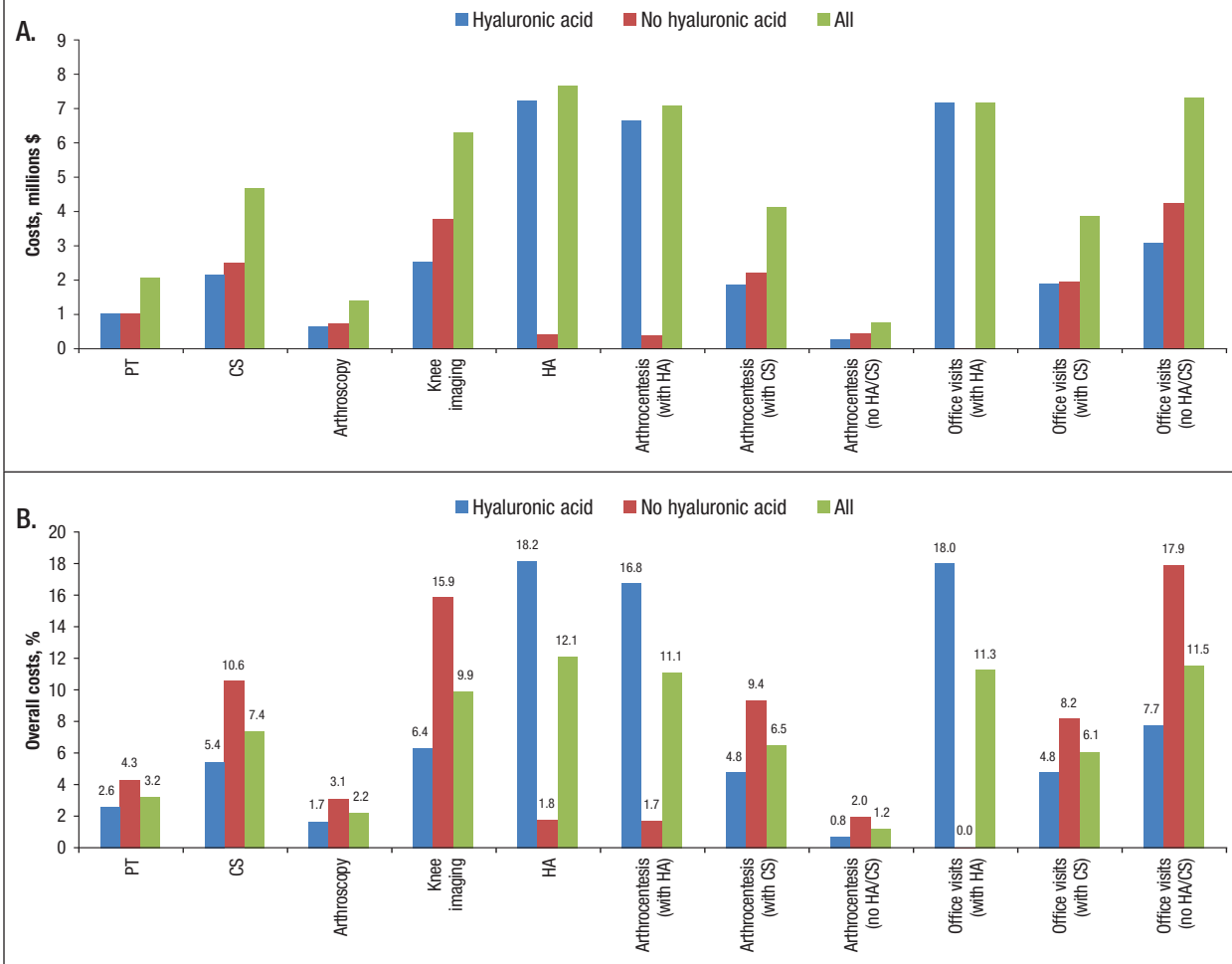
The mean time from diagnosis to knee arthroplasty was 11.5 (±13.6) months for the 24,604 patients who did not receive hyaluronic acid and 20.5 (±15.2) months for the 10,861 patients who received hyaluronic acid. The median time to knee arthroplasty was 10.7 months longer for patients who received hyaluronic acid (16.4 months; interquartile range [IQR], 8.2-29.7 months) than for patients who did not receive hyaluronic acid (5.7 months; IQR, 2.0-16.2 months). For the patients who received hyaluronic acid, the mean time from the first hyaluronic acid injection to knee arthroplasty was 11.8 (±14.9) months (median, 8.4 months; IQR, 4-18 months; **Table 2**).

Of the hyaluronic acid cohort, nearly 10% had knee arthroplasty within 2 months of receiving hyaluronic acid injection. When extended to the 3-month period after the initial hyaluronic acid injection, 16.9% of patients who received hyaluronic acid had knee arthroplasty. Of the remaining patients who received hyaluronic acid with knee arthroplasty, the mean time between the first hyaluronic acid injection and knee arthroplasty was 15.3 ±12.6 months (median, 10.7 months; IQR, 5.9-20.9; Table 2).

Discussion

In patients with knee OA in the Medicare population, nonarthroplasty therapies and knee arthroplasty accounted for similar proportions of the treatment costs

Figure 4 Knee OA–Related Cost Categories for Patients in the 12 Months Before Knee Arthroplasty, by (A) Dollar Amount, and (B) by Percent[a]



[a]Arthrocentesis and office visits with hyaluronic acid or corticosteroid have been included in the hyaluronic acid and corticosteroid categories.
CS indicates corticosteroid injections; HA, hyaluronic acid; OA, osteoarthritis; PT, physical therapy.

for knee OA, with hyaluronic acid comprising a small fraction (5.6%) of the total knee OA–related costs. Of the patients who received hyaluronic acid, 23.7% subsequently had knee arthroplasty during the study period. Of the patients who received hyaluronic acid and subsequently had knee arthroplasty, the hyaluronic acid injection resulted in only 1.8% of the overall knee OA treatment costs compared with knee arthroplasty, which contributed 76.6% of the knee OA–related cost.

The patients who received hyaluronic acid and then had knee arthroplasty had increases in their median knee OA–related costs approximately ≥1 years after their first hyaluronic acid injection, which likely reflects having knee arthroplasty. They also incurred almost 11 times greater knee OA–related costs over the 4-year period after being diagnosed with knee OA than their hyaluronic acid injection counterparts who did not have knee arthroplasty. Among all patients who had knee arthroplasty, those who previously received treatment with hyaluronic acid had a longer time to knee arthroplasty.

Unlike Bedard and colleagues, who reported that 12-month presurgical knee OA–related costs could be reduced by 29.3% by omitting hyaluronic acid,[5] in our present study, we found that hyaluronic acid only accounted for 12.1% of the knee OA–related costs during the 12-month period. The difference in the relative cost contributions may lie in the previous analysis including only noninpatient knee OA–related costs in a mix of privately insured and Medicare or Medicaid Advantage cohorts in the earlier study[5] compared with all therapies in the Medicare cohort in our study.

By contrast, Cohen and colleagues also included in-

Table 2 Time Between Patients Receiving First Hyaluronic Acid Injection and a Subsequent Knee Arthroplasty

Treatment group	Patients, N	First hyaluronic acid injection to knee arthroplasty: Average (SD), mo	25th percentile, mo	Median, mo	75th percentile, mo
Hyaluronic acid with subsequent knee arthroplasty	10,861	11.8 (±14.9)	4	8.4	18
Subsequent knee arthroplasty, by month 3 of hyaluronic acid injection	1836	2.2 (±0.6)	1.8	2.3	2.7
Subsequent knee arthroplasty, after month 3 of hyaluronic acid injection	9025	15.3 (±12.6)	5.9	10.7	20.9

SD indicates standard deviation.

patient and procedural costs in their evaluation of the charges within the 2-year period before total knee arthroplasty for Medicare and privately insured patients, albeit without the total knee arthroplasty costs.[6] When inpatient and procedural costs were included, injections only contributed approximately 3% to the per-patient mean charges compared with approximately 60% from procedures and anesthesia and approximately 25% from imaging.

Similarly, Berger and colleagues found in the PharMetrics Patient-Centric claims data that hyaluronic acid treatments represented only 1.2% of the mean healthcare costs per patient in the 2 years before, but not including knee arthroplasty, whereas outpatient care, pharmacotherapy, and inpatient care represented approximately 45%, 21%, and 19%, respectively.[22] Overall, our study showed that hyaluronic acid treatment accounted for 5.6% of the overall cost of knee OA care within the study period, which was comparable in cost contributions from physical therapy, corticosteroid injections, knee imaging, and non–hyaluronic acid or non–corticosteroid-related office visits.

In our study, knee arthroplasty accounted for the majority of the knee OA–related costs (51%) compared with other therapies, such as hyaluronic acid, which only accounted for 5.6% of the knee OA–related costs. The disparity is more apparent for patients who received hyaluronic acid injections and subsequently had knee arthroplasty, in which hyaluronic acid contributed only 1.8% of the knee OA–related costs compared with 76.6% from knee arthroplasty.

In addition, patients who received hyaluronic acid and did not have knee arthroplasty incurred less than 10% of the knee OA–related costs than patients who had knee arthroplasty. Our findings quantified the lag time to knee arthroplasty with corresponding knee OA–related cost reduction to the healthcare system.

In recent years there has been increasing emphasis on value-based healthcare, such as the cost study by Bedard and colleagues, who noted that pre–knee arthroplasty treatment costs could be reduced by up to 45% if only therapies recommended by the AAOS clinical practice guidelines were used.[5] Although the AAOS guidelines were not the only guidelines that recommended against the use of hyaluronic acid in the treatment of knee OA, conflicting recommendations from other guidelines have provided uncertain or no recommendations for the use of hyaluronic acid or have deemed it an appropriate intervention under certain scenarios.[23-28]

These inconsistent recommendations result from variability in the methodologies used in evidence inclusion, evidence assessment, recommendation formulation, and work group composition,[23] and further do not account for the use of multimodal treatments and the potential for hyaluronic acid and corticosteroid therapies to decrease the use of other medications, such as NSAIDs and opioids.[29-31]

If the AAOS guidelines and other guidelines that recommend against the use of hyaluronic acid are adopted by payers, this proved and cost-effective treatment option will become unavailable for many patients, which may lead to earlier progression to knee arthroplasty. A substantial portion of patients with knee OA are not candidates for knee arthroplasty, whereas patients with early-stage OA would benefit from treatment options that delay the need for knee arthroplasty. Many patients also have contraindications for other first-line therapies, such as pain medications.[32]

Furthermore, recent knee OA research has identified only minimal relief from acetaminophen,[33] only short-term benefit and early toxicity from NSAIDs,[34] increased risk for mortality in the first year of treatment with tramadol,[35] and has raised questions about the advisability of corticosteroid injections, because of concerns regarding progressive cartilage damage through repeated injections.[36,37] These concerns regarding the risk-benefit impact of other traditionally recommended nonoperative treatments for knee OA, coupled with the cost-based results of our study, emphasize the potential negative impact on value-based nonsurgical care of patients with knee OA from insurance coverage decisions that limit patient access to hyaluronic acid injections.

Our findings showed a longer time to knee arthroplasty for patients who received treatment with hyaluronic acid versus patients who did not receive hyaluronic acid, with a corresponding lag in knee OA–related treatment cost increases as a result of having knee arthroplasty. The patients who received hyaluronic acid and did not have knee arthroplasty within 3 months of receiving their first hyaluronic acid injection (ie, patients who were allowed

appropriate time for the optimal effects of hyaluronic acid treatment) also had an extended time of approximately 15 months between their first injection and having knee arthroplasty.

Extending the time to knee arthroplasty can provide patients more time to modify their habits or risk factors before surgery; for example, patients may be able to wean off of opioid treatment,[15-17] lose weight,[18-20] regulate their glucose intake,[19,20] or cease nicotine or tobacco use,[19,20] which, in turn, can help to reduce the risk for poorer outcomes after knee arthroplasty.

The time horizon is also an important consideration when controlling healthcare costs. A potential benefit is the one-time cost-savings from delaying knee arthroplasty, which provides a lower discounted procedure cost.[38] Cost utility research also does not support early total knee arthroplasty over late total knee arthroplasty.[39] Extending the time to knee arthroplasty can have economic value because Medicare patients may switch to other capitated plans by the time they have surgery, so that the knee OA–related cost is shared between several plans. There may also be patient attrition before the need truly arises for knee arthroplasty or any subsequent revision knee arthroplasty.[38]

By contrast, other studies have reported that a longer presurgery waiting time can have a negative impact on patient outcomes after surgery.[40,41] It is unclear if the possible lack of the use of other intervening therapies or addressing modifiable risk factors during the waiting period could have negatively affected patients who waited for surgery. If patients were able to avoid knee arthroplasty by using other treatment modalities, it may provide economic benefit to the healthcare system. For example, our findings showed that patients who received hyaluronic acid injections and did not have knee arthroplasty incurred less than 10% of the median knee OA–related costs than patients who received hyaluronic acid and had knee arthroplasty.

We also observed that a substantial proportion of patients who received hyaluronic acid had knee arthroplasty within a short period after the first injection (10% within 2 months). This time frame may be of concern, because it does not allow for an appropriate evaluation of the effectiveness of a hyaluronic acid injection, which is most effective at 8 weeks after the first injection.[42] Thus, patients who may have improved to a degree with hyaluronic acid injection, which led them to opt out of surgery, might instead have had surgery before gaining the benefit of maximum relief if they waited long after their hyaluronic acid injection.

Furthermore, although we were unable to determine the severity of knee OA among the population studied (eg, Kellgren-Lawrence grade) because we used administrative claims data, the close temporal association between hyaluronic acid injection and knee arthroplasty suggests that either patients with end-stage knee OA were receiving hyaluronic acid injection (in which case the use of hyaluronic acid is questionable, because its treatment effects are less robust in late-stage disease[43]), or patients with very mild disease were undergoing knee arthroplasty, which has been shown to lead to poorer functional outcomes from surgery.[44]

It is also theoretically possible that the hyaluronic acid injections were given to the knee opposite to that on which the replacement was performed, perhaps to aid in postoperative recovery. Nevertheless, the data suggest that patients who received hyaluronic acid injection and did not have knee arthroplasty within 3 months after the first hyaluronic acid injection had an extended time (mean, 15.3 months) between their first injection and the knee arthroplasty procedure. We did not evaluate the combined use of a corticosteroid with hyaluronic acid, but this treatment strategy has demonstrated improved earlier pain relief[45,46] and has been associated with an extended time to knee arthroplasty.[13]

Limitations

This study has several limitations. The current results were based on Medicare patients and may not reflect younger and/or privately insured patients with knee OA nor patients with HMO coverage. Because of the use of administrative claims data, the severity of knee OA and the reasons for selecting different therapies for individual patients could not be examined.

Because the patient population in our study focused on elderly patients, this study might have included an increased proportion of patients with more severe OA, which makes them more likely to be candidates for knee arthroplasty, compared with younger patients. It was also unclear if the majority of patients who did not have knee arthroplasty were not candidates for knee arthroplasty or were able to avoid arthroplasty because they had relief from the use of other therapies.

The economic burden evaluated in this study was from direct costs to payers, which underestimated the true knee OA–related costs, because it does not include any indirect knee OA–related costs. The indirect knee OA–related costs can potentially exceed the direct costs associated with knee OA in some healthcare systems.[21]

Furthermore, the costs were examined from a descriptive nature, without statistical analyses, but they still provide useful data about trends and cost estimates.

The relationship between comorbidities and knee OA–related costs was not within the scope of the present study; the relative effectiveness of various therapies was also not considered.

The knee OA–related cost contributions of pharmaceutical drugs also could not be examined in this study, because the 5% Medicare data set did not contain that information.

At the time of the initiation of this study, data from 2015 were the most recent Medicare data available, hence costs may have changed.

Conclusion

This study used a large sample of elderly patients with knee OA to provide a real-world understanding of the direct knee OA–related costs related to various interventions. Intra-articular hyaluronic acid is a nonsurgical option that reduces pain, improves functionality, and may aid in delaying the time to knee arthroplasty.

Our study showed that in patients who received hyaluronic acid injections and had knee arthroplasty during the study period, hyaluronic acid treatment resulted in only 1.8% of their overall knee OA–related treatment costs with a delay for surgical intervention by 15 months. Overall, this study demonstrates that hyaluronic acid injections can reduce payers' costs of treatment related to patients with knee OA and can delay the need for knee arthroplasty.

Funding Source

Funding for this study was provided by Ferring Pharmaceuticals, Inc.

Author Disclosure Statement

Dr Niazi is an employee of Ferring Pharmaceuticals. Mr Lau is an employee of Exponent, which provides consulting services to Ferring Pharmaceuticals and to many other pharmaceutical companies. Dr Kurtz is an employee and shareholder of Exponent, which provides consulting services to Ferring Pharmaceuticals and to many other pharmaceutical companies; he has also received royalties from Elsevier. Dr Ong is an employee and shareholder of Exponent, which provides consulting services to Ferring Pharmaceuticals and to many other pharmaceutical companies. Dr Concoff is a speaker for and a consultant to Flexion Therapeutics and Exagen, and a consultant to UCB. Dr Malanga and Dr Kidd have no conflicts of interest to report.

References

1. Arthritis Foundation. *Arthritis By the Numbers: Book of Trusted Facts and Figures 2020*. www.arthritis.org/getmedia/73a9f02d-7f91-4084-91c3-0ed0b11c5814/ABTN-2020-FINAL.pdf. Accessed April 24, 2020.
2. Losina E, Katz JN. Total joint replacement outcomes in patients with concomitant comorbidities: a glass half empty or half full? *Arthritis Rheum*. 2013;65:1157-1159.
3. Losina E, Walensky RP, Kessler CL, et al. Cost-effectiveness of total knee arthroplasty in the United States: patient risk and hospital volume. *Arch Intern Med*. 2009;169:1113-1121; discussion 1121-1122.
4. American Academy of Orthopaedic Surgeons. *Treatment of Osteoarthritis of the Knee: Evidence-Based Guideline*. 2nd ed. Rosemont, IL; 2013. www.aaos.org/globalassets/quality-and-practice-resources/osteoarthritis-of-the-knee/osteoarthritis-of-the-knee-2nd-edition-clinical-practice-guideline.pdf. Accessed March 15, 2018.
5. Bedard NA, Dowdle SB, Anthony CA, et al. The AAHKS Clinical Research Award: what are the costs of knee osteoarthritis in the year prior to total knee arthroplasty? *J Arthroplasty*. 2017;32(9 suppl):S8-S10.e1.
6. Cohen JR, Bradley AT, Lieberman JR. Preoperative interventions and charges before total knee arthroplasty. *J Arthroplasty*. 2016;31:2730-2735.e7.
7. Losina E, Paltiel AD, Weinstein AM, et al. Lifetime medical costs of knee osteoarthritis management in the United States: impact of extending indications for total knee arthroplasty. *Arthritis Care Res (Hoboken)*. 2015;67:203-215.
8. Kurtz SM, Ong KL, Lau E, Bozic KJ. Impact of the economic downturn on total joint replacement demand in the United States: updated projections to 2021. *J Bone Joint Surg Am*. 2014;96:624-630.
9. Incacio MCS, Paxton EW, Graves SE, et al. Projected increase in total knee arthroplasty in the United States: an alternative projection model. *Osteoarthritis Cartilage*. 2017;25:1797-1803. Epub ahead of print.
10. Altman R, Fredericson M, Bhattacharyya SK, et al. Association between hyaluronic acid injections and time-to-total knee replacement surgery. *J Knee Surg*. 2016;29:564-570.
11. Altman R, Lim S, Steen RG, Dasa V. Hyaluronic acid injections are associated with delay of total knee replacement surgery in patients with knee osteoarthritis: evidence from a large U.S. health claims database. *PLoS One*. 2015;10:e0145776. Erratum in: *PLoS One*. 2016;11:e0148591.
12. Delbarre A, Amor B, Bardoulat I, et al. Do intra-articular hyaluronic acid injections delay total knee replacement in patients with osteoarthritis – a Cox model analysis. *PLoS One*. 2017;12:e0187227.
13. Ong KL, Anderson AF, Niazi F, et al. Hyaluronic acid injections in Medicare knee osteoarthritis patients are associated with longer time to knee arthroplasty. *J Arthroplasty*. 2016;31:1667-1673.
14. Ong KL, Runa M, Lau E, Altman R. Is intra-articular injection of Synvisc associated with a delay to knee arthroplasty in patients with knee osteoarthritis? *Cartilage*. 2019;10:423-431.
15. Bedard NA, Pugely AJ, Westermann RW, et al. Opioid use after total knee arthroplasty: trends and risk factors for prolonged use. *J Arthroplasty*. 2017;32:2390-2394.
16. Cancienne JM, Patel KJ, Browne JA, Werner BC. Narcotic use and total knee arthroplasty. *J Arthroplasty*. 2018;33:113-118.
17. Nguyen LCL, Sing DC, Bozic KJ. Preoperative reduction of opioid use before total joint arthroplasty. *J Arthroplasty*. 2016;31(9 suppl):S282-S287.
18. Bookman JS, Schwarzkopf R, Rathod P, et al. Obesity: the modifiable risk factor in total joint arthroplasty. *Orthop Clin North Am*. 2018;49:291-296.
19. DeFroda SF, Rubin LE, Jenkins DR. Modifiable risk factors in total joint arthroplasty: a pilot study. *R I Med J (2013)*. 2016;99:28-31.
20. Kee JR, Mears SC, Edwards PK, Barnes CL. Modifiable risk factors are common in early revision hip and knee arthroplasty. *J Arthroplasty*. 2017;32:3689-3692.
21. Salmon JH, Rat AC, Sellam J, et al. Economic impact of lower-limb osteoarthritis worldwide: a systematic review of cost-of-illness studies. *Osteoarthritis Cartilage*. 2016;24:1500-1508.
22. Berger A, Bozic K, Stacey B, et al. Patterns of pharmacotherapy and health care utilization and costs prior to total hip or total knee replacement in patients with osteoarthritis. *Arthritis Rheum*. 2011;63:2268-2275.
23. Altman RD, Schemitsch E, Bedi A. Assessment of clinical practice guideline methodology for the treatment of knee osteoarthritis with intra-articular hyaluronic acid. *Semin Arthritis Rheum*. 2015;45:132-139.
24. American College of Rheumatology. American College of Rheumatology position statement: intra-articular hyaluronic acid injection in osteoarthritis of the knee. www.rheumatology.org/Portals/0/Files/Viscosupplementation.pdf. Accessed March 15, 2018.
25. Bannuru RR, Vaysbrot EE, McIntyre LF. Did the American Academy of Orthopaedic Surgeons osteoarthritis guidelines miss the mark? *Arthroscopy*. 2014;30:86-89.
26. Bruyère O, Cooper C, Pelletier JP, et al. A consensus statement on the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) algorithm for the management of knee osteoarthritis—from evidence-based medicine to the real-life setting. *Semin Arthritis Rheum*. 2016;45(4 suppl):S3-S11.
27. McAlindon TE, Bannuru RR, Sullivan MC, et al. OARSI guidelines for the non-surgical management of knee osteoarthritis. *Osteoarthritis Cartilage*. 2014;22:363-388. Erratum in: *Osteoarthritis Cartilage*. 2015;23:1026-1034.
28. Trojian TH, Concoff AL, Joy SM, et al. AMSSM scientific statement concerning viscosupplementation injections for knee osteoarthritis: importance for individual patient outcomes. *Clin J Sport Med*. 2016;26:1-11.

29. Altman RD, Rosen JE, Bloch DA, Hatoum HT. Safety and efficacy of retreatment with a bioengineered hyaluronate for painful osteoarthritis of the knee: results of the open-label Extension Study of the FLEXX Trial. *Osteoarthritis Cartilage*. 2011;19:1169-1175.
30. McIntyre LF, Beach W, Bhattacharyya S, et al. Impact of hyaluronic acid injections on pain management medications utilization. *Am J Pharm Benefits*. 2017;9:195-199.
31. Waddell DD, Bricker DC. Clinical experience with the effectiveness and tolerability of hylan G-F 20 in 1047 patients with osteoarthritis of the knee. *J Knee Surg*. 2006;19:19-27.
32. Conrozier T, Monfort J, Chevalier X, et al. EUROVISCO recommendations for optimizing the clinical results of viscosupplementation in osteoarthritis. *Cartilage*. 2020;11:47-59.
33. Leopoldino AO, Machado GC, Ferreira PH, et al. Paracetamol versus placebo for knee and hip osteoarthritis. *Cochrane Database Syst Rev*. 2019;2:CD013273.
34. Osani MC, Vaysbrot EE, Zhou M, et al. Duration of symptom relief and early trajectory of adverse events for oral NSAIDs in knee osteoarthritis: a systematic review and meta-analysis. *Arthritis Care Res (Hoboken)*. 2020 May;72:641-651.
35. Zeng C, Dubreuil M, LaRochelle MR, et al. Association of tramadol with all-cause mortality among patients with osteoarthritis. *JAMA*. 2019;321:969-982.
36. McAlindon TE, LaValley MP, Harvey WF, et al. Effect of intra-articular triamcinolone vs saline on knee cartilage volume and pain in patients with knee osteoarthritis: a randomized clinical trial. *JAMA*. 2017;317:1967-1975.
37. Wernecke C, Braun HJ, Dragoo JL. The effect of intra-articular corticosteroids on articular cartilage: a systematic review. *Orthop J Sports Med*. 2015;3:2325967115581163.
38. Fortin PR, Penrod JR, Clarke AE, et al. Timing of total joint replacement affects clinical outcomes among patients with osteoarthritis of the hip or knee. *Arthritis Rheum*. 2002;46:3327-3330.
39. Mari K, Dégieux P, Mistretta F, et al. Cost utility modeling of early vs late total knee replacement in osteoarthritis patients. *Osteoarthritis Cartilage*. 2016;24:2069-2076.
40. Desmeules F, Dionne CE, Belzile É, et al. Waiting for total knee replacement surgery: factors associated with pain, stiffness, function and quality of life. *BMC Musculoskelet Disord*. 2009;10:52.
41. Lizaur-Utrilla A, Martinez-Mendez D, Miralles-Muñoz FA, et al. Negative impact of waiting time for primary total knee arthroplasty on satisfaction and patient-reported outcome. *Int Orthop*. 2016;40:2303-2307.
42. Bannuru RR, Natov NS, Dasi UR, et al. Therapeutic trajectory following intra-articular hyaluronic acid injection in knee osteoarthritis–meta-analysis. *Osteoarthritis Cartilage*. 2011;19:611-619.
43. Nicholls M, Shaw P, Niazi F, et al. The impact of excluding patients with end-stage knee disease in intra-articular hyaluronic acid trials: a systematic review and meta-analysis. *Adv Ther*. 2019;36:147-161.
44. Stone OD, Duckworth AD, Curran DP, et al. Severe arthritis predicts greater improvements in function following total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc*. 2017;25:2573-2579.
45. Ertürk C, Altay MA, Altay N, et al. Will a single periarticular lidocaine–corticosteroid injection improve the clinical efficacy of intraarticular hyaluronic acid treatment of symptomatic knee osteoarthritis? *Knee Surg Sports Traumatol Arthrosc*. 2016;24:3653-3660.
46. Ozturk C, Atamaz F, Hepguler S, et al. The safety and efficacy of intraarticular hyaluronan with/without corticosteroid in knee osteoarthritis: 1-year, single-blind, randomized study. *Rheumatol Int*. 2006;26:314-319.