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A Retrospective Cohort Analysis of the Impact of Osteoarthritis on Disability Leave, Workers' Compensation Claims, and Healthcare Payments

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Objectives: Examine short-term disability (STD) and workers' compensation (WC) associated leave and wage replacements, and overall direct healthcare payments, among employees with osteoarthritis (OA) versus other chronically painful conditions; quantifying the impact of opioid use. **Methods:** Analysis of employees with more than or equal to two STD or WC claims for OA or pre-specified chronically painful conditions (control) in the IBM MarketScan Research Databases (2014 to 2017). **Results:** The OA cohort ($n = 144{,}355$) had an estimated +1.2 STD days, +$152 STD payments, and +$1410 healthcare payments relative to the control cohort ($n = 392{,}639$; $P < 0.001$). WC days/payments were similar. Differences were partially driven by an association between opioid use, increased STD days/payments, and healthcare payments observed in pooled cohorts ($P < 0.001$). **Conclusions:** OA is associated with high STD days/payments and healthcare payments. Opioid use significantly contributes to these and this should be considered when choosing treatment.

Keywords: chronic pain, disability, employee, opioid, osteoarthritis, United States

BACKGROUND

Osteoarthritis (OA) is one of the most common musculoskeletal disorders globally and is increasing in prevalence within the United States (U.S.).[1–6] OA is also an important cause of chronic pain and functional disability, characterized by varying degrees of joint pain and stiffness.[1–3,7] Furthermore, it is a frequent cause of increased healthcare resource utilization and reductions in work productivity.[5,6,8–11] The burden of OA has been consistently shown to increase with disease severity, including a strong association between severity and declining work productivity, increasing work absence, and increasing unemployment.[12–15]

Though their use is discouraged in treatment guidelines, opioids are one of the most common prescription medications provided to employees with OA in the U.S.[16–20] Yet, opioids provide minimal improvements in pain and function for employees with OA and are associated with further increases in healthcare costs/utilization and lost wages.[21–27]

In the U.S., many employers provide short-term disability (STD) benefits for employees who are temporarily unable to work due to an illness, injury, pregnancy, or recovery from a medical procedure.[28,29] Most employers are also required to provide workers' compensation (WC) insurance that pays medical expenses and wage replacements to employees for injuries or illness that are caused by work-related activities.[30] These programs are beneficial to both employers and employees, as they provide employees with a guaranteed payment to cover the financial impact of injuries or illness and fulfill employers' obligation to compensate employees for lost time at work and healthcare costs.

Currently, little is known about the relative impact of OA on these types of disability leave in the U.S. The impact of opioid use on these outcomes is also not well characterized. Specific objectives of this retrospective, observational cohort study were to compare STD and WC leave days/payments and direct healthcare payments between employees with OA versus other chronically painful conditions in a U.S. working adult population. The effect of opioid use on these specific outcomes was also assessed.

METHODS

Data Source

This was a retrospective, non-interventional database analysis using anonymized patient-level claims data from the IBM MarketScan Research Databases (MarketScan Commercial Claims and Encounters [CCAE] and Health and Productivity Management [HPM] databases). Data are from a non-random sample of large employers' healthcare/disability insurance claims from employees geographically dispersed throughout the U.S.

The CCAE database contains indicators for annual and monthly health benefits enrollment (including demographics, plan sponsor information, and health plan design attributes). It also includes claims for inpatient, outpatient, and prescription pharmacy treatments. Treatment claims data include information on dates of services, one or more diagnoses (International Classification of Diseases and Related Health Problems [ICD], Ninth Revision [ICD-9] or Tenth Revision [ICD-10]), therapeutic class (for pharmacy claims), and payment details.

The HPM database contains indicators of annual eligibility, and claims for, STD and WC benefits. WC claims data include the primary diagnosis (ICD-9 or ICD-10) and date of injury or illness for which benefits were authorized, the number of lost workdays (if

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Ethical approvals: This was an analysis of data from an anonymized database; therefore, ethics approval was not required. The principles of the Declaration of Helsinki were followed.

Clinical significance: Osteoarthritis is a notable cause of short-term disability, work productivity loss, and increased healthcare payments relative to other chronically painful conditions. Much of this derives from the strong association between opioid use, work productivity loss, and increased healthcare payments. Treatment patterns should be reappraised with an aspiration to enhance employability.

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any), and the value of wage replacements and healthcare payments associated with the claim. STD claims data include the primary diagnosis (ICD-9 or ICD-10) and date of injury or illness for which benefits were authorized, the number of lost workdays, and the value of wage replacements.

Employee Sample

Unique individuals were identified in each database based on a common enrollee identification number. Individuals (aged 18 to 64 years) were considered for inclusion in the study based on their eligibility for benefits. They must have been the primary beneficiary (ie, the employee) and eligible for medical, pharmacy, STD, and WC benefits for all months from January 2014 through December 2017 (48 months consecutively).

Cohorts

Eligible employees were divided into two cohorts based on their treatment history for OA or other pre-specified painful conditions (ICD-9 and ICD-10 primary or secondary/additional diagnosis codes listed in Table 1). Employees were included in the OA cohort if they had two or more treatment claims with primary or supplemental diagnoses of OA. Employees were included in the other chronically painful conditions (control) cohort if they had two or more treatment claims with a diagnosis for a pre-specified painful condition at least 30 days apart.[31] Employees not meeting the criteria for either cohort were excluded. For the purposes of developing statistical weights and controlling for confounding characteristics (described below), we created an indicator variable for each of the conditions included in the control cohort.

The index date for each employee was the first claim with an eligible diagnosis code. Each employee record was divided to provide a pre-index period (January 1, 2014 to index date) and a post-index observation period (index date to December 31, 2017).

Dependent Variables

Dependent variables were the cumulative lost workdays due to STD or WC (including 0 lost days for WC claims that only incurred medical or other payments), STD payments (wage replacement), WC payments (sum of wage replacements, medical, and other payments including legal fees and vocational rehabilitation), and healthcare payments (sum of inpatient, outpatient, and prescription drug claim payments) during the observation period.

To ensure that we did not overestimate the influence of OA on STD outcomes—for example, after adjusting for the confounding influences of age and sex, we assumed no mechanism for OA to influence STD claims for conditions such as pregnancy or cancer—we only included STD claims with a diagnosis for OA, a different pre-specified painful condition, or for a condition found in the WC claims data (typically injuries and musculoskeletal conditions). This resulted in the exclusion of 64% of the STD claims that accounted for 61% of STD lost workdays and 63% of STD payments.

Prescription Medications

Employees' prescribed use of acetaminophen, duloxetine, hyaluronic acid, tramadol, non-tramadol opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and corticosteroids was identified by the U.S. Food and Drug Administration national drug code included with each prescription pharmacy claim. Employees with a prescription were coded as a 1 for that drug, and a 0 otherwise. For statistical weighting (described below), medications were assessed prior to the index period. For our final models, we included only medications prescribed for at least 3% of employees in both cohorts combined—opioids, NSAIDs, acetaminophen, and tramadol. Given our general interest in the relationship between opioid use, disability, and healthcare payments, we measured medication use at any time during the study period for use in our regression models.

Health Plan Type

We calculated an employee's health plan type based on the number of months prior to the observation period they were enrolled in a preferred provider organization, health maintenance organization, point-of-service, or high-deductible health plan. We then converted the number of months into a proportion of the pre-observation period. While an employee could have been enrolled in more than one type of health plan, 88% were continuously enrolled in the same type of plan.

Comorbidities

We used diagnosis information (ICD-9 and ICD-10 codes) from inpatient and outpatient claims to create dichotomous variables indicating whether an employee received treatment for several comorbid conditions during the pre-observation period. These were obesity, diabetes mellitus, hypertension, hyperlipidemia, sleeping problems, anxiety, or depression (ICD codes listed in Table 1).

Demographics

Our models controlled for available employee and employer characteristics. Employer characteristics were limited to the industries of the plan sponsors included in the CCAE and HPM datasets that have both WC and STD data. Industries were durable goods manufacturing; non-durable goods manufacturing; transportation, communications and utilities; services; finance, insurance and real estate; and retail trade.

Employee demographics were sex (male or female), age, and Census region (North Central, Northeast, South, and West). Indicators for whether an employee was unionized (yes or no) and whether they were salaried or paid hourly were also given.

Statistical Method

All analyses were conducted using Stata version 14.2 (StataCorp, TX).

Statistical Weighting

One challenge when conducting analyses of observational data is that ''assignment'' to either a treatment or control group is non-random and may be associated with the outcome of interest.[32] In this case, selection bias complicates the interpretation of effect sizes. We tried to address the risk of selection bias with inverse probability of treatment weighting (IPTW) to balance the measured characteristics across the OA and control cohorts.[33]

Univariate Analysis

We report the proportions of employees with a claim for WC, STD, or either type during the observation period in the supplemental material. We compared the differences across the cohorts using a test of independence from two-way contingency tables. We also report proportions for the most common diagnoses.

Regression Analyses

We conducted a series of multivariable regression models to estimate employees' outcomes during the observation period. Each outcome was estimated using a separate model that included an indicator of the cohort, indicators of prescription medication use, non-OA pain and other comorbid conditions, health plan information, industry, and employee demographics. Additionally, each model also controlled for employees' outcomes prior to the index period. For example, the model estimating WC lost workdays during the index period included a measure of WC lost workdays observed prior to the index period.

For the WC and STD lost workdays and payments models, we treated the outcomes as over-dispersed count data and used a negative binomial estimator. Healthcare payments showed a strong positive skew and initial regression models produced non-normally

TABLE 1. Diagnosis Codes for the OA and Control Cohort Conditions and Comorbidities

Diagnoses	ICD-9 Codes	ICD-10 Codes
OA cohort		
OA	715.x, 721.0x–721.4x	M13.1x, M13.8x, M15.x–M19.x, M47.0x, M47.11–M47.16, M47.21–M47.28, M47.811–M47.818, M47.891–M47.898
Pre-specified other chronically painful conditions (control) cohort		
Abdominal pain	550.x–553.x, 789.0x, 789.6x	K40.x–K46.x, R10.x (excluding R10.83)
Arthropathy	696.0, 710–719	A18.01, A18.02, A52.16, D86.86, E08.610, E08.618, E09.610, E09.618, E10.610, E10.618, E11.610, E11.618, E13.610, E13.618, L40.5x, M00.x, M01.x, M02.x, M06.4, M07.x, M11.0x, M11.8x, M11.9, M12.5x, M12.8x, M12.9, M13.0, M14.6x, M14.8x, M36.1, M36.2, M36.3, M36.4
Back pain	307.89, 724.1, 724.2, 724.5, 724.6	M48.06, M48.07, M54, M62.830, M96.1, M99.23, M99.33, M99.43, M99.53, M99.63, M99.73
Cervical radiculopathy	722.0, 723.4, 724.4, 729.2, 732.2, 732.3, 732.6	M43.6, M53.0, M53.1, M54.00, M54.01, M54.02, M54.11, M54.12, M54.13, M54.2
Diabetic neuropathy	249.x, 250.60, 357.2, 548, 648.03, 648.04	E08.40, E08.42, E09.40, E09.42, E10.4x, E10.610, E11.4x, E11.610, E13.4x, E13.610
Fibromyalgia	729.1	M79.7
Genitourinary pain	256, 257, 603, 604, 620.0, 625.2, 625.9, 626, 789.00	E28.8, E29.8, N94.89, R10.2
Gout	247.01, 247.02, 247.03, 247.10, 247.11, 247.68, 247.81, 247.82, 274.00, 274.19, 274.9	M1A.0x, M1A.2x–M1A.9x, M10.0x–M10.2x
Headache (non-migraine)	339, 784.0, 784.9	G44.x, R51
Joint pain (other than OA)	714.30, 719.0, 719.4–719.9, 720, 725	A18.01, M08.1, M25.5x, M35.3, M45.x, M46.0x, M46.1x, M46.5x, M46.8x, M48.8x, M49.x, M79.0, M79.646
Limb pain	337.21, 337.22, 353.6, 354.0, 354.4, 355.71, 725, 726, 727, 728, 729, 729.5	G54.6, G54.7, G56.4x, G57.7x, M60–M63, M65–M67, M70–M72, M75–M77, M79.6x
Lumbar radiculopathy	723.4, 724.4, 729.2	M54.15, M54.16, M54.17
Migraine	346	G43.x
Multiple sclerosis	340, 341, 357.0	G35
Muscular dystrophy	259, 333.90, 359.1, 359.2	G71.0, G71.11, G71.13, G71.2
Neuralgia	350.1, 723.3, 724.4, 729.2	G50.0, M54.10, M79.2
Other neuropathy	320, 330, 337.9, 340, 350, 355.1, 355.9, 356.4, 357.1–357.7, 359, 701.0, 710.1, 724.3	A52.15, G13.0, G13.1, G57.1x, G60.0, G60.1, G60.3, G60.8, G60.9, G61.1, G61.81, G61.89, G61.9, G62.x, G63, G64, G65.x, G90.09, G99.0, M05.5x, M34.83, M54.3x, M54.4x
Other/chronic pain	338.x, 780.96	F45.42, G89.0, G89.21, G89.29, G89.4, R52
Painful bladder syndrome	595, 596, 752, 752.62, 788.43, 788.99	N30.1x, R35.0
Post-herpetic neuropathy	053.12, 532.0	B02.2x
Rheumatoid arthritis	714.x	M05.x, M06.x (excluding M06.4), M08.x, M12.0x
Spinal cord injury	952.x	S14.0x, S14.1x, S24.0x, S24.1x, S34.0x, S34.1x, S34.3x
Surgically induced pain	338.18, 998.89	G89.18, G89.22, G89.28
Comorbidities of interest (both cohorts)		
Obesity	278.0x–278.03x, 783.1, V45.86, V55.3	E65.x, E66.x–E67.0
Diabetes mellitus	250.x	E08.x–E13.x
Hypertensive disease	401.x–405.x	I10.x–I16.x
Lipoid metabolism disorder	272.x	E78.x
Sleep-related conditions	307.4x, 327.x, 327.0x–327.1x, 347.x, 780.5x, V69.4	F51.x, G47.x
Anxiety	300.0x, 300.1x, 300.2x, 300.3–300.7, 300.8x	F40.x, F41.x, F44.x, F45.x
Depression	296.2x, 296.3x, 311.x	F32.x, F33.x
Obsessive compulsive disorder	300.3	F42.x, R468.1
Post-traumatic stress disorder	309.81	F43.1x

OA, osteoarthritis.

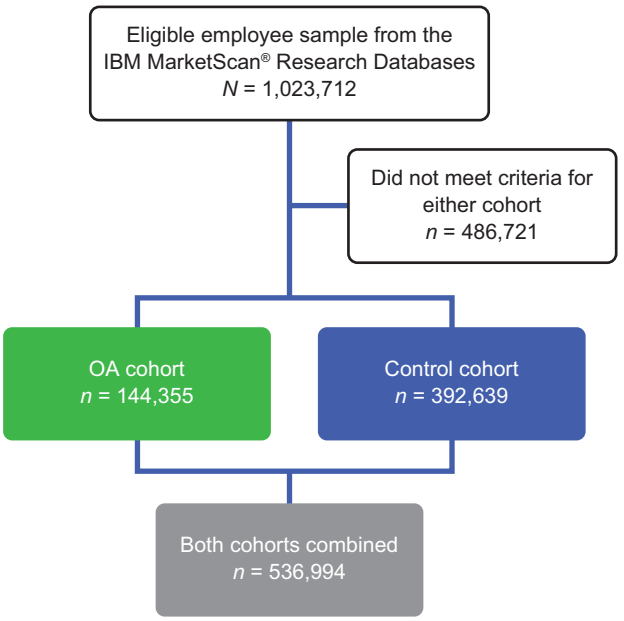

FIGURE 1. Employee selection. Control cohort comprises employees with a broad range of other (non-OA) chronically painful conditions. OA, osteoarthritis.

distributed residuals. For these reasons, we transformed the outcome variable by the natural log and estimated using ordinary least squares regression.

Because we were interested in whether use of prescription opioids influences WC and STD outcomes differently for the OA and control cohort, each model included an interaction term for the combination of cohort and opioids indicator variables. We report the overall OA cohort and opioids coefficients (to reflect the sample means of each group), and the linear combinations of the main and interaction action effects for the four sample populations represented by the interaction. We express the coefficients from the negative binomial estimators as incidence rate ratios (IRR; ie, the proportional difference in expected counts) for a one-unit change in the covariate and describe estimated counts for selected outcomes.

RESULTS

Based on the selection criteria, 1,023,712 employees were identified in the IBM MarketScan Research Databases as eligible for inclusion. Of these, 144,355 met the inclusion criteria in the OA cohort and 392,639 met the inclusion criteria for the control cohort (Fig. 1).

Cohort Comparison Before Weighting

Standardized differences between means describe the balance between cohorts. Maximum standardized differences of about 10% indicate a reasonable level of balance for a given covariate between cohorts.[32,34] Before weighting, the original OA and control cohorts were unbalanced on most of the covariates (Table 2). Importantly, the original OA cohort had higher pre-index use of prescription pain medications than the original control cohort, ranging from around 2.5-times higher incidence of opioid (42% vs 17%) and acetaminophen (5% vs 2%) use to six-times higher incidence of tramadol (12% vs 2%) use during the observation period. Employees with OA were, on average, older and had higher rates of comorbidities, including many of the control cohort conditions.

Cohort Comparison After Weighting

IPTW improved the balance of the sample across the study covariates (Table 2). After IPTW, five diagnosis variables—indicators for abdominal pain, genitourinary pain, non-OA joint pain, back pain, and limb pain—had an absolute standardized difference of at least 10%. The log of pre-index medical treatment payments had a standardized difference of −20.7%, whereas the standardized difference of the untransformed variable was 0.9%. The change in the direction of the standardized difference after log transforming reflects a longer righthand skew within the OA cohort (skew = 32.6) than in the control cohort (skew = 22.6).

The weighted mean index date across both cohorts occurred on March 29, 2015, suggesting an average observation period of about 33 months and a pre-index period of about 16 months. Of particular interest for the current study, after weighting, around one in five employees across both cohorts had at least one pre-index opioid (21%) or NSAID prescription (18%). The most common painful conditions for inclusion in the control group were non-OA joint pain, limb pain, and back pain. Taken together, 86% of the control cohort had at least one of these conditions, compared with 72% of the OA cohort. During the pre-index period, the weighted OA cohort had lower mean WC and STD days and WC and STD payments than the control cohort (Table 2). Healthcare payments for the OA cohort were skewed rightward, resulting in marginally higher mean payments.

Univariate Analyses

Supplemental Table 1, http://links.lww.com/JOM/A996, shows the proportions of employees with any WC or STD claim during the observation period and with the most common diagnoses associated with each type of claim.

Regression Analyses

In the IPTW-weighted multiple regression models (Table 3), we were principally interested in coefficients for the OA cohort, use of opioids, and the interaction between these covariates.

Given the OA cohort × opioids interaction included in the models, Table 4 reports the overall OA cohort and opioids coefficients and the linear combinations of the main and interaction action effects for the four sample populations represented by the interaction.

Cohort Comparison

On average, employees in the OA cohort were estimated to have 12% fewer WC days and 16% lower WC payments than employees in the control cohort over the observation period (Table 4; payments were $P < 0.05$). Employees in both cohorts were estimated to have about 0.6 WC days and $184 to $219 in WC payments, with an overall average of $199 (±$25; Fig. 2A and B).

Estimated incidence rates for STD days over the observation period were 90% higher in the OA cohort (Table 4; $P < 0.001$), while STD payments were about twice as high (Table 4; $P < 0.001$). The models estimated about 1.4 STD days and $160 STD payments for the control cohort over observation, and 1.2 additional STD days and $152 in additional STD payments for the OA cohort (Fig. 2C and D).

Healthcare payments were estimated to be about 9% higher among the OA cohort (Table 4; $P < 0.001$); estimated at $17,027 (±$198) for the OA cohort and $15,617 (±$116) for the control cohort (Fig. 2E).

Impact of Opioids

Opioid use was a significant predicator for all outcomes. Employees prescribed opioids had significantly higher estimated lost workdays and payments (Table 4). For lost workdays, the overall estimated IRR for opioids was about 2.4 for WC and 5.5 for STD. IRR values for payments were 2.2 for WC and 7.2 for STD. Estimated healthcare payments were twice as high for employees prescribed opioids than payments for employees without opioid

TABLE 2. Summary of the Original and IPTW Cohorts

	Original Cohorts			IPTW Cohorts		
	OA Cohort	**Control Cohort**	**Standardized Difference Before IPTW**	**OA Cohort**	**Control Cohort**	**Standardized Difference After IPTW**
Employees, *n*	144,355	392,639	–	144,355	392,639	–
Prescribed medications, %						
Opioids	42	17	55.4	20	22	−4.0
NSAIDs	41	12	70.1	17	19	−4.0
Acetaminophen	5	2	18.6	2	3	−0.9
Tramadol	12	2	39.0	4	4	−0.2
Index date	Sept 16, 2015	Feb 23, 2015		Mar 20, 2015	Apr 9, 2015	
Comorbidities of interest, %						
Obesity	28	20	18.3	20	22	−5.6
Diabetes	18	14	12.8	14	15	−1.0
Hypertensive disease	51	38	26.2	39	41	−3.7
Lipoid disorder	54	44	20.0	45	47	−4.0
Sleeping problems	27	19	20.0	19	20	−3.5
Anxiety	19	17	5.8	15	17	−4.4
Depression	14	11	9.9	10	11	−3.7
Pre-specified chronically painful conditions in the control cohort, %						
Abdominal pain	30	31	−3.4	23	29	−13.6
Arthropathy	7	2	23.5	3	3	−0.5
Cervical radiculopathy	31	18	31.3	19	20	−4.4
Fibromyalgia	8	5	14.4	4	5	−3.1
Genitourinary pain	20	22	−4.6	14	20	−14.7
Headache (non-migraine)	15	14	2.8	11	14	−8.0
Lumbar radiculopathy	23	9	38.6	11	11	−1.6
Migraine	7	7	2.5	5	6	−5.6
Neuralgia	13	5	26.3	6	7	−1.3
Neuropathy	16	9	22.5	9	10	−2.8
Chronic pain, other	18	7	34.0	9	9	−1.9
Joint pain (other than OA)	70	41	61.3	43	48	−10.3
Back pain	55	41	28.8	38	43	−10.4
Limb pain	72	57	31.6	51	59	−17.2
Bladder pain	7	6	2.5	5	6	−4.9
Demographics						
Age, yrs	51	45	66.1	47	47	1.3
Female, %	40	39	2.0	35	39	−7.3
Industry of employment, %						
Manufacturing, durable goods	43	40	5.6	41	42	−0.2
Transportation, communications, utilities	22	22	0.3	22	22	2.2
Services	15	15	−0.3	14	15	−0.6
Manufacturing, nondurable goods	7	9	−8.1	8	9	−1.8
Finance, insurance, real estate	8	9	−1.2	8	9	−0.8
Retail trade	4	5	−0.9	4	4	0.0
Health plan type, based on % months enrolled						
PPO	52	51	3.0	51	51	−1.2
High-deductible	31	34	−6.5	34	33	1.6
POS	5	5	2.6	5	5	−0.7
HMO	8	7	2.8	8	8	0.4
Employee characteristics, %						
Unionized	29	24	10.5	25	26	−1.2
Hourly	53	48	10.7	49	49	−1.0
Employee region, %						
North Central	30	27	6.3	27	28	−0.5
Northeast	12	14	−4.3	13	14	−1.5
South	45	44	2.3	44	44	1.2
West	13	16	−7.1	15	15	0.4
Pre-index outcomes, mean						
WC days	2.3	0.9	6.2	1.3	2.8	−6.4
WC payments	$627	$252	6.9	$325	$1255	−17.0
STD days	4.5	0.5	20.6	1.5	6.5	−25.7
STD payments	$473	$36	16.3	$151	$175	−0.9
Healthcare payments	$13,222	$3965	34.4	$5719	$5489	0.9
Healthcare payments (log)	8.0	5.8	76.5	5.7	6.3	−20.7

Lower absolute standardized differences in means indicate a greater balance among cohorts for a specific covariate. Standardized differences no greater than 10% to 25% have been proposed as indicating acceptable balance. Control cohort comprises employees with a broad range of other (non-OA) chronically painful conditions.

HMO, health maintenance organization; IPTW, inverse probability treatment weighting; NSAIDs, nonsteroidal anti-inflammatory drugs; OA, osteoarthritis; POS, point-of-service; PPO, preferred provider organization; STD, short-term disability; WC, workers' compensation.

TABLE 3. Regression Coefficients and Standard Errors for Weighted Regression Models

$N = 536{,}994$ (Pooled Cohorts), Coefficient (Standard Error)	WC Days	WC Payments	STD Days	STD Payments	Healthcare Payments (Log)
Osteoarthritis	−0.143 (0.140)	−0.164 (0.147)	0.359 (0.076)***	0.295 (0.100)**	−0.045 (0.010)***
Opioids	0.864 (0.104)***	0.814 (0.091)***	1.410 (0.036)***	1.57 (0.057)***	0.595 (0.008)***
Osteoarthritis × opioids	0.032 (0.186)	−0.025 (0.193)	0.558 (0.084)***	0.745 (0.110)***	0.260 (0.015)***
NSAIDs	0.321 (0.095)***	0.276 (0.083)***	0.142 (0.041)***	0.130 (0.051)*	0.046 (0.008)***
Acetaminophen	0.333 (0.214)	0.066 (0.105)	0.438 (0.072)***	0.550 (0.110)***	0.209 (0.014)***
Tramadol	0.396 (0.119)***	0.449 (0.086)***	0.660 (0.047)***	0.707 (0.054)***	0.265 (0.009)***
Index date	−0.001 (0.000)***	−0.001 (0.000)***	0 (0.000)***	0 (0.000)***	−0.001 (0.000)***
Obesity	−0.236 (0.094)*	0.053 (0.087)	0.098 (0.041)*	0.078 (0.051)	0.129 (0.009)***
Diabetes mellitus	0.070 (0.130)	0.071 (0.086)	0.139 (0.063)*	0.110 (0.074)	0.296 (0.009)***
Hypertensive disease	0.197 (0.091)*	0.064 (0.070)	0.103 (0.047)*	0.121 (0.058)*	0.169 (0.008)***
Lipoid metabolism disorder	0.024 (0.093)	−0.085 (0.075)	−0.193 (0.051)***	−0.258 (0.065)***	0.071 (0.008)***
Sleeping problems	0.097 (0.113)	0.070 (0.080)	−0.003 (0.047)	0.003 (0.058)	0.225 (0.007)***
Anxiety	0.060 (0.127)	−0.022 (0.088)	0.228 (0.064)***	0.244 (0.093)**	0.107 (0.009)***
Depression	0.121 (0.121)	0.084 (0.096)	0.197 (0.051)***	0.231 (0.074)**	0.146 (0.009)***
Abdominal pain	0.088 (0.104)	0.003 (0.081)	0.211 (0.038)***	0.236 (0.056)***	0.366 (0.008)***
Arthropathy	0.228 (0.306)	0.189 (0.179)	0.206 (0.077)**	0.215 (0.094)*	0.445 (0.014)***
Cervical radiculopathy	0.199 (0.140)	0.034 (0.106)	0.122 (0.059)*	0.104 (0.078)	0.123 (0.010)***
Fibromyalgia	−0.165 (0.133)	−0.247 (0.098)*	−0.273 (0.053)***	−0.423 (0.071)***	−0.067 (0.010)***
Genitourinary pain	0.003 (0.099)	0.089 (0.081)	−0.077 (0.051)	−0.029 (0.067)	0.132 (0.008)***
Headache (non-migraine)	0.221 (0.117)	0.141 (0.092)	0.129 (0.065)*	0.136 (0.093)	0.150 (0.010)***
Lumbar radiculopathy	0.096 (0.173)	0.155 (0.135)	0.410 (0.053)***	0.448 (0.073)***	0.095 (0.009)***
Migraine	−0.240 (0.129)	−0.207 (0.106)	0.180 (0.066)**	0.107 (0.082)	0.096 (0.010)***
Neuralgia	−0.222 (0.166)	−0.129 (0.129)	−0.088 (0.064)	−0.082 (0.081)	−0.053 (0.010)***
Neuropathy	0.072 (0.170)	0.058 (0.122)	0.436 (0.068)***	0.478 (0.089)***	0.208 (0.009)***
Chronic pain, other	−0.067 (0.121)	0.089 (0.109)	0.437 (0.040)***	0.504 (0.058)***	0.198 (0.007)***
Joint pain	0.152 (0.090)	0.185 (0.075)*	0.481 (0.038)***	0.532 (0.053)***	0.187 (0.007)***
Back pain	0.088 (0.090)	0.064 (0.083)	−0.022 (0.045)	−0.028 (0.056)	0.020 (0.008)*
Limb pain	0.205 (0.097)*	0.105 (0.092)	0.419 (0.045)***	0.570 (0.059)***	0.183 (0.008)***
Bladder pain	0.344 (0.166)*	0.371 (0.150)*	−0.008 (0.060)	−0.105 (0.080)	0.148 (0.010)***
Age	0.025 (0.005)***	0.022 (0.007)***	0.018 (0.003)***	0.033 (0.004)***	0.012 (0.001)***
Female	0.198 (0.108)	−0.032 (0.087)	−0.026 (0.048)	0.009 (0.068)	0.121 (0.009)***
Manufacturing, durable goods	0.910 (0.160)***	0.558 (0.152)***	0.706 (0.077)***	0.443 (0.097)***	0.007 (0.012)
Transportation, communications, utilities	1.998 (0.162)***	0.713 (0.154)***	0.420 (0.086)***	−0.036 (0.120)	−0.034 (0.013)**
Services	2.464 (0.174)***	−0.439 (0.156)**	−0.317 (0.103)**	−0.358 (0.148)*	0.107 (0.014)***
Finance, insurance, real estate	0.462 (0.269)	−0.552 (0.292)	0.588 (0.127)***	−0.004 (0.137)	0.102 (0.015)***
PPO (enrolled months)	1.143 (0.227)***	0.942 (0.179)***	−0.009 (0.063)	0.387 (0.087)***	0.052 (0.020)*
High-deductible	1.093 (0.245)***	0.609 (0.187)**	−0.166 (0.076)*	0.009 (0.103)	−0.078 (0.021)***
POS	−0.680 (0.269)*	−0.098 (0.205)	0.187 (0.092)*	1.319 (0.113)***	0.168 (0.027)***
HMO	0.372 (0.255)	0.610 (0.193)**	−0.004 (0.080)	0.017 (0.124)	−0.081 (0.023)***
Unionized	1.090 (0.121)***	0.625 (0.102)***	0.338 (0.063)***	0.222 (0.077)**	−0.026 (0.013)*
Hourly	2.125 (0.105)***	2.008 (0.102)***	1.483 (0.051)***	0.980 (0.075)***	−0.065 (0.009)***
North Central region	−0.443 (0.121)***	−0.049 (0.108)	0.034 (0.053)	0.235 (0.060)***	0.050 (0.009)***
Northeast region	0.511 (0.185)**	0.251 (0.109)*	0.287 (0.068)***	0.436 (0.090)***	0.125 (0.015)***
West region	0.214 (0.132)	0.721 (0.239)**	0.015 (0.088)	−0.129 (0.113)	0.051 (0.012)***
WC days: pre-index	0.008 (0.002)***				
WC payments: pre-index		0 (0.000)			
STD days: pre-index			0.002 (0.001)		
STD payments: pre-index				0 (0.000)***	
Healthcare payments: pre-index (log)					0.087 (0.002)***
Constant	14.840 (2.800)***	20.568 (2.203)***	6.665 (1.210)***	8.747 (1.600)***	36.415 (0.233)***
lnalpha	5.228 (0.023)***	5.264 (0.014)***	3.613 (0.011)***	4.634 (0.010)***	
Pseudo R-squared	0.023	0.007	0.029	0.009	
R-squared					0.495
N	536,994	536,994	536,994	536,994	536,994
Estimation method	nbreg	nbreg	nbreg	nbreg	regression

Control cohort comprises employees with a broad range of other (non-OA) chronically painful conditions.

HMO, health maintenance organization; nbreg, negative binomial regression; NSAIDs, nonsteroidal anti-inflammatory drugs; OA, osteoarthritis; POS, point-of-service; PPO, preferred provider organization; STD, short-term disability; WC, workers' compensation.

*$P < 0.05$.

**$P < 0.01$.

***$P < 0.001$.

prescriptions. On average, employees not prescribed opioids had about 0.4 WC days and about 0.8 STD days. Employees prescribed opioids had an additional 0.5 WC days and an additional 3.8 STD days (Fig. 2A and C). Employees prescribed opioids also had an additional $163 in WC payments, $520 in additional STD payments, and $12,239 in additional healthcare payments (Fig. 2B, D, and E).

Since NSAIDs, acetaminophen, and tramadol were included as controls in the models, the strict opioid comparison was to

TABLE 4. Exponentiated Main and Linear Interaction Coefficients From Multivariate Regression Models

	WC Days	WC Payments	STD Days	STD Payments	Healthcare Payments (log)
Main effects					
OA cohort	0.881	0.838*	1.898***	1.956***	1.090***
Opioids	2.414***	2.228***	5.519***	7.159***	2.084***
Interactions					
OA cohort (no opioids)	0.867	0.848	1.433***	1.343**	0.956***
OA cohort (with opioids)	0.895	0.828	2.502***	2.829***	1.240***

See Table 3 for linear coefficients. Results for WC and STD days and payments represent incidence rate ratios from negative binomial regression estimates. Results for healthcare payments are interpreted as the percentage change in the geometric mean. Control cohort comprises employees with a broad range of other (non-OA) chronically painful conditions.
OA, osteoarthritis; STD, short-term disability; WC, workers' compensation.
*$P < 0.05$.
**$P < 0.01$.
***$P < 0.001$.

employees not prescribed any of the most common pain management drugs. Wald chi-squared tests conducted after each model indicated that the coefficient for opioids was significantly higher ($P \leq 0.05$ in each case) than the coefficients for the other drugs.

Cohort and Opioids Interactions

Opioid use was a particularly strong predictor of higher STD days/payments and healthcare payments in the OA cohort (Table 4). Among employees not prescribed opioids, estimated incidence rates for STD days were about 43% higher in the OA cohort ($P < 0.001$). By comparison, the IRR is 150% higher among employees prescribed opioids. Comparable results for STD payments were of similar magnitudes.

Among employees not prescribed opioids, estimated healthcare payments were about 4% lower for the OA cohort than for the control cohort. By comparison, among employees prescribed opioids, estimated healthcare payments were 24% higher in the OA cohort. This suggests that the positive and significant overall association between the OA cohort and healthcare payments is driven by employees prescribed opioids.

DISCUSSION

Findings from this retrospective, non-interventional database analysis demonstrate that U.S. employees with OA had an estimated 90% higher incidence of STD days, 96% higher STD payments, and 9% higher healthcare payments than a control cohort of employees with other chronically painful conditions. While WC lost workdays were generally uncommon, they were 12% fewer and associated with 16% lower WC payments among employees with OA. These data demonstrate the particular importance of OA as a cause of disability lost workdays, associated wage replacements, and healthcare payments in the context of other chronically painful conditions. A combined cohort analysis additionally showed all outcomes to be higher among employees who took opioids versus those who did not. The effect of opioid use was found to be a major driver of increased disability days and payments in employees with OA.

The negative association between OA, work productivity, and overall economic burden has been demonstrated in a number of studies, but usually in comparison with the general population of employees.[8,11,35–37] The absolute number of additional disability days and payments incurred by employees with OA varies considerably with methodology (region, population, data source, joints affected by OA, modeling, etc) and is not easily compared between studies. Using data from the 2009 U.S. National Health and Wellness Survey, DiBonaventura et al[12] showed rate ratios for absenteeism and presenteeism in employees with OA to range from 1.04 to 1.86 relative to those without OA, depending on disease severity. These findings are similar to our findings of around twice the risk of STD days and STD payments compared with employees with other chronically painful conditions.

Our study showed a lower risk of WC days and payments (~0.8 times risk) among employees with OA versus other chronically painful conditions. However, we also found almost no WC claims for OA in either cohort. Employees with chronic pain might be less likely to claim WC than employees in the general population due to the "healthy worker effect"—where "unhealthy" employees (those with physical limitations) are less likely to take physically demanding jobs, thus are less likely to incur work-related injuries and also find it easier to stay at work after an injury (eg, on light duties) because of the nature of their job and workplace.[38,39] This effect might be occurring more commonly in our cohort with other chronically painful conditions (mainly non-OA joint pain, back pain, or limb pain). It has been suggested that factors other than comorbidities, such as age, can have a considerable role to play in the costs associated with work-related injuries; however, age was controlled for in our models.[40]

While the estimated mean annual number of disability days associated with OA may not be as high as other chronic conditions, such as spinal injury or limb loss, the high prevalence of OA means that these lost days can have a large cumulative impact on employers.[6,41] We found that employees with OA incurred an extra $1410 (9%) in estimated healthcare payments (inpatient, outpatient, and prescription drug claims) compared with employees with other chronically painful conditions over a mean observation period of 33 months. This is in the context of the known high costs of treating chronic pain conditions, indicating that OA is associated with a particularly notable economic burden.[42] While the impact of OA versus the general employee population has been demonstrated, the relative impact versus other chronically painful conditions has not been well studied.[6,8,10,11,15,21,24,36,39,41,43] Prior to our study, we are only aware of Jetha et al[44] who identified arthritis to be associated with the longest duration of disability (STD and long-term disability claims combined) when compared with seven other chronic conditions (diabetes, hypertension, coronary artery disease, depression, low back pain, chronic pulmonary disease, or cancer) in a large sample from a U.S. private insurance claims database.

Opioids continue to be prescribed to patients with OA despite the number of annual prescriptions declining in the U.S. as a result of efforts to address the opioid epidemic.[45] Treatment guidelines generally recommend against the use of opioids in patients with OA due to limited evidence of a positive impact on pain or function; however, treatment options are limited.[16–27,46] A major finding from our study was that, across cohorts, opioid use was associated with significantly higher number of estimated disability days and payments of all types. The magnitude of the differences exceeded those between cohorts (2.4- and 2.2-times higher WC days and

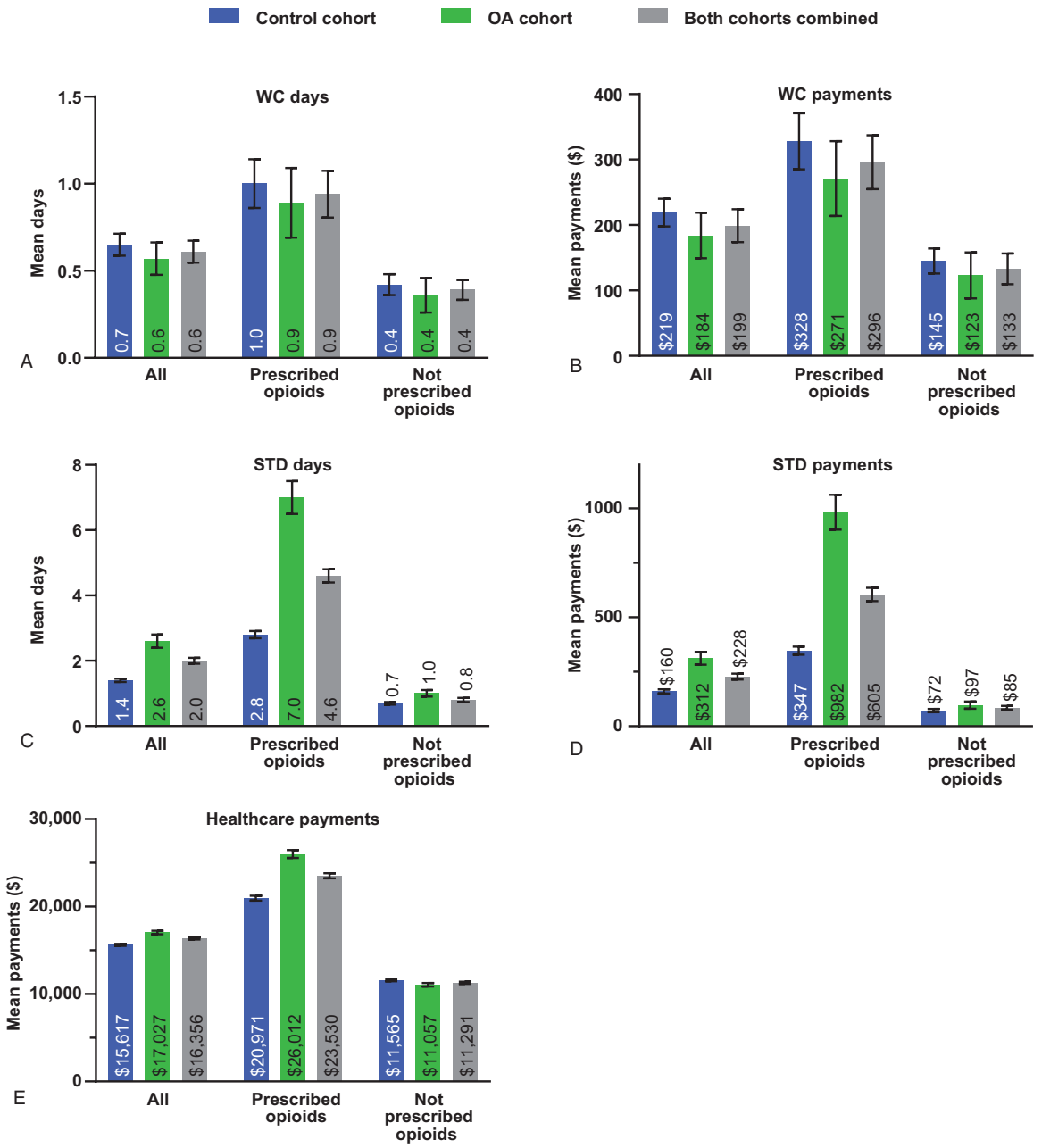

FIGURE 2. Estimated outcomes by cohort and opioid use. Control cohort comprises employees with a broad range of other (non-OA) chronically painful conditions. Shows mean ± 95% confidence interval from a multivariate regression model. Indicates opioids prescribed during the study period. OA, osteoarthritis; STD, short-term disability; WC, workers' compensation.

payments; 5.5- and 7.2-times higher STD days and payments; 2.1-times healthcare payments). Analysis of the interaction between opioids and the OA cohort showed that, in our data, opioid use was a major driver of the additional STD days, STD payments, and healthcare payments observed in employees with OA versus employees with other chronically painful conditions. Further study evaluating the impact of opioids in more detail is warranted, that is, by medication, number of prescriptions, or morphine milligram equivalents. Previous literature has demonstrated links between opioid use, decreased work productivity, and higher costs when used to treat chronic noncancer pain, such as low back pain.[47,48] Our study is one of few to focus specifically on people with OA. Zhao et al[21] previously studied U.S. Medical Expenditure Panel Survey data from U.S. adults with OA and found opioid use to have a strong association with direct and indirect costs, more so than the level of pain interference with activities. Wei et al[24] studied U.S. claims data and electronic health records and found opioid use in patients with OA to be independently associated with higher healthcare resource use and costs. Similarly, an observational longitudinal assessment of patients with OA and chronic pain in Spain found meaningful increases in resource use and costs after starting opioids, despite modest reductions in pain.[23] The reasons that opioids are associated

with negative outcomes in people with chronic pain (including pain due to OA) are likely multifactorial. Opioids have been shown to provide no additional benefit in pain-related function over non-opioid medications for people with back pain and OA and are associated with more adverse effects.[22] The known adverse effect profile and risk of addiction associated with opioids likely contributes to the negative work productivity outcomes observed in our analysis.

Notable strengths of our study include the large sample size and the long length of follow-up (mean observation of ~33 months), which exceeds most similar studies. The breadth of data captured is also a major strength. We believe that our comparison strategy (OA vs other chronically painful conditions) is unique, allowing the dissection of the impact of OA on work productivity to be carved out in comparison to a large group of chronically painful conditions.

Our study approach also has several limitations. Firstly, IBM MarketScan data are derived from a non-random sample of large employers' healthcare and disability insurance benefits and are not generalizable to the population of U.S. employees working for small or mid-sized employers. Secondly, our cohort does not include those with more severe and limiting chronic pain. We required continuous employment and benefit enrollment from 2014 to 2017, so those who subsequently left employment (and lost their insurance coverage) due to chronic pain are not included in our analysis. Thirdly, because data are based on treatment-seeking/benefit claiming behavior, they may not be comprehensive with regards to health conditions that did not trigger treatment or a claim. We do not have records of reportable on-the-job injuries that did not result in claims for medical treatment or wage replacement. This may have resulted in an undercount of less serious or ''near-miss'' incidents where OA or opioids were contributing factors. Fourthly, supplemental sources of health condition data such as self-reported health risk assessments, values obtained by lab tests, details of disease severity or duration, or data about patient characteristics, such as socioeconomic status (eg, household income), race/ethnicity, and granular geographic location (eg, zip code or census block) are not available but may have associations with our outcomes. This could contribute to omitted variable bias. Additionally, WC and STD claims do not capture the full burden of illness, and lost workdays as a result of absenteeism or presenteeism (without a STD or WC claim) are not included. We are further aware that STD benefit offerings vary by state, insurer, industry, and company; however, these factors are not detailed in the source database. A final but important limitation is related to the designation of other conditions qualifying for inclusion in the control cohort. This cohort was developed to allow the relative impact of OA to be measured and included a broad range of chronically painful conditions. These conditions may not be clinically or qualitatively similar to OA insofar as they increase the risks of WC or STD experience. The selections may also limit the ability to generate feasible propensity scores if the employees' underlying demographic profiles differ from employees with OA. It is notable that joint pain was the most common condition in both the control and OA cohorts. In the control cohort there is a possibility that some of the claims for chronic joint pain (and other conditions) represent undiagnosed OA. This would bias our findings towards the null and therefore true differences between the cohorts may be larger than stated.

CONCLUSION

In the context of increasing OA prevalence, our findings add to the growing evidence of a significant association between OA, opioid use, and increased work absence. OA was associated with a higher incidence of work productivity loss, and higher short-term disability and healthcare payments, than a comparator cohort including a broad selection of other chronically painful conditions. The use of opioids was a key driver in this finding. We highlight the importance of understanding and considering therapies prescribed to employees with OA and chronic musculoskeletal pain so that their ability to work is supported.

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REFERENCES

1. James SL, Abate D, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392:1789–1858.
2. Safiri S, Kolahi A-A, Smith E, et al. Global, regional and national burden of osteoarthritis 1990-2017: a systematic analysis of the Global Burden of Disease Study 2017. *Ann Rheum Dis*. 2020;79:819–828.
3. Hunter DJ, March L, Chew M. Osteoarthritis in 2020 and beyond: a Lancet Commission. *Lancet*. 2020;396:1711–1712.
4. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet*. 2019;393:1745–1759.
5. Zhao X, Shah D, Gandhi K, et al. Clinical, humanistic, and economic burden of osteoarthritis among noninstitutionalized adults in the United States. *Osteoarthritis Cartilage*. 2019;27:1618–1626.
6. Lo J, Chan L, Flynn S. A systematic review of the incidence, prevalence, costs, and activity and work limitations of amputation, osteoarthritis, rheumatoid arthritis, back pain, multiple sclerosis, spinal cord injury, stroke, and traumatic brain injury in the United States: a 2019 update. *Arch Phys Med Rehabil*. 2021;102:115–131.
7. Murray CJ, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2197–2223.
8. Menon J, Mishra P. Health care resource use, health care expenditures and absenteeism costs associated with osteoarthritis in US healthcare system. *Osteoarthritis Cartilage*. 2018;26:480–484.
9. Jordan K, Clarke AM, Symmons DP, et al. Measuring disease prevalence: a comparison of musculoskeletal disease using four general practice consultation databases. *Br J Gen Pract*. 2007;57:7–14.
10. Bitton R. The economic burden of osteoarthritis. *Am J Manag Care*. 2009;15:S230–S235.
11. Hubertsson J, Petersson IF, Thorstensson CA, Englund M. Risk of sick leave and disability pension in working-age women and men with knee osteoarthritis. *Ann Rheum Dis*. 2013;72:401–405.
12. Dibonaventura MD, Gupta S, McDonald M, Sadosky A, Pettitt D, Silverman S. Impact of self-rated osteoarthritis severity in an employed population: cross-sectional analysis of data from the national health and wellness survey. *Health Qual Life Outcomes*. 2012;10:30.
13. Nakata K, Tsuji T, Vietri J, Jaffe DH. Work impairment, osteoarthritis, and health-related quality of life among employees in Japan. *Health Qual Life Outcomes*. 2018;16:64.
14. Sadosky AB, Bushmakin AG, Cappelleri JC, Lionberger DR. Relationship between patient-reported disease severity in osteoarthritis and self-reported pain, function and work productivity. *Arthritis Res Ther*. 2010;12:R162.
15. Nalamachu S, Robinson RL, Viktrup L, et al. Pain severity and healthcare resource utilization in patients with osteoarthritis in the United States. *Postgrad Med*. 2021;133:10–19.
16. Basedow M, Esterman A. Assessing appropriateness of osteoarthritis care using quality indicators: a systematic review. *J Eval Clin Pract*. 2015;21:782–789.
17. Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartilage*. 2019;27:1578–1589.
18. Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. *Arthritis Care Res (Hoboken)*. 2020;72:149–162.
19. Nalamachu SR, Robinson RL, Viktrup L, et al. Multimodal treatment patterns for osteoarthritis and their relationship to patient-reported pain severity: a cross-sectional survey in the United States. *J Pain Res*. 2020;13:3415–3425.

20. Dziedzic KS, Allen KD. Challenges and controversies of complex interventions in osteoarthritis management: recognizing inappropriate and discordant care. *Rheumatology (Oxford)*. 2018;57(suppl):iv88–iv98.
21. Zhao X, Shah D, Gandhi K, et al. The association of pain interference and opioid use with healthcare utilization and costs, and wage loss among adults with osteoarthritis in the United States. *J Med Econ*. 2019;22:1192–1201.
22. Krebs EE, Gravely A, Nugent S, et al. Effect of opioid vs nonopioid medications on pain-related function in patients with chronic back pain or hip or knee osteoarthritis pain: the SPACE randomized clinical trial. *JAMA*. 2018;319:872–882.
23. Sicras-Mainar A, Tornero-Tornero C, Vargas-Negrín F, Lizarraga I, Rejas-Gutierrez J. Health outcomes and costs in patients with osteoarthritis and chronic pain treated with opioids in Spain: the OPIOIDS real-world study. *Ther Adv Musculoskelet Dis*. 2020;12:1759720X20942000.
24. Wei W, Gandhi K, Blauer-Peterson C, Johnson J. Impact of pain severity and opioid use on health care resource utilization and costs among patients with knee and hip osteoarthritis. *J Manag Care Spec Pharm*. 2019;25:957–965.
25. Osani M, Lohmander S, Bannuru R. Is there any role for opioids in the management of OA? [abstract]. *Arthritis Rheumatol*. 2019;71(suppl 10):1575.
26. Osani MC, Lohmander LS, Bannuru RR. Is there any role for opioids in the management of knee and hip osteoarthritis? A systematic review and meta-analysis. *Arthritis Care Res (Hoboken)*. 2021. doi:10.1002/acr.24363.
27. Shah D, Zhao X, Wei W, et al. A longitudinal study of the association of opioid use with change in pain interference and functional limitations in a nationally representative cohort of adults with osteoarthritis in the United States. *Adv Ther*. 2020;37:819–832.
28. Nathan S. The Balance Careers. Short-term Disability Basics [Internet]; 2019. Available at: https://www.thebalancecareers.com/short-term-disability-basics-1177839. Accessed March 24, 2021.
29. U.S. Department of Labor. Employment laws: medical and disability-related leave [Internet]; 2021. Available at: https://www.dol.gov/agencies/odep/publications/fact-sheets/employment-laws-medical-and-disability-related-leave. Accessed April 1, 2021.
30. U.S. Department of Labor. Workers' compensation [Internet]; 2021. Available at: https://www.dol.gov/general/topic/workcomp. Accessed March 24, 2021.
31. Lamerato LE, Dryer RD, Wolff GG, et al. Prevalence of chronic pain in a large integrated healthcare delivery system in the U.S.A. *Pain Pract*. 2016;16:890–898.
32. Garrido MM, Kelley AS, Paris J, et al. Methods for constructing and assessing propensity scores. *Health Serv Res*. 2014;49:1701–1720.
33. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011;46:399–424.
34. Zhang Z, Kim HJ, Lonjon G, Zhu Y. Balance diagnostics after propensity score matching. *Ann Transl Med*. 2019;7:16.
35. Kotlarz H, Gunnarsson CL, Fang H, Rizzo JA. Osteoarthritis and absenteeism costs: evidence from US National Survey Data. *J Occup Environ Med*. 2010;52:263–268.
36. Berger A, Hartrick C, Edelsberg J, Sadosky A, Oster G. Direct and indirect economic costs among private-sector employees with osteoarthritis. *J Occup Environ Med*. 2011;53:1228–1235.
37. Laires PA, Canhão H, Rodrigues AM, Eusébio M, Gouveia M, Branco JC. The impact of osteoarthritis on early exit from work: results from a population-based study. *BMC Public Health*. 2018;18:472.
38. Li CY, Sung FC. A review of the healthy worker effect in occupational epidemiology. *Occup Med (Lond)*. 1999;49:225–229.
39. Hermans J, Koopmanschap MA, Bierma-Zeinstra SM, et al. Productivity costs and medical costs among working patients with knee osteoarthritis. *Arthritis Care Res (Hoboken)*. 2012;64:853–861.
40. Smith PM, Bielecky A, Ibrahim S, et al. How much do preexisting chronic conditions contribute to age differences in health care expenditures after a work-related musculoskeletal injury? *Med Care*. 2014;52:71–77.
41. Ma VY, Chan L, Carruthers KJ. Incidence, prevalence, costs, and impact on disability of common conditions requiring rehabilitation in the United States: stroke, spinal cord injury, traumatic brain injury, multiple sclerosis, osteoarthritis, rheumatoid arthritis, limb loss, and back pain. *Arch Phys Med Rehabil*. 2014;95:986.e1–995.e1.
42. Phillips CJ. The cost and burden of chronic pain. *Rev Pain*. 2009;3:2–5.
43. Neogi T. The epidemiology and impact of pain in osteoarthritis. *Osteoarthritis Cartilage*. 2013;21:1145–1153.
44. Jetha A, Besen E, Smith PM. Comparing the relationship between age and length of disability across common chronic conditions. *J Occup Environ Med*. 2016;58:485–491.
45. National Center for Drug Abuse Statistics. Opioid epidemic: addiction statistics [Internet]; 2020. Available at: https://drugabusestatistics.org/opioid-epidemic/. Accessed August 13, 2021.
46. Noble M, Treadwell JR, Tregear SJ, et al. Long-term opioid management for chronic noncancer pain. *Cochrane Database Syst Rev*. 2010;2010:Cd006605.
47. Webster BS, Verma SK, Gatchel RJ. Relationship between early opioid prescribing for acute occupational low back pain and disability duration, medical costs, subsequent surgery and late opioid use. *Spine (Phila Pa 1976)*. 2007;32:2127–2132.
48. Eriksen J, Sjøgren P, Bruera E, Ekholm O, Rasmussen NK. Critical issues on opioids in chronic non-cancer pain: an epidemiological study. *Pain*. 2006;125:172–179.

