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Time Trends in Opioid Use Disorder Hospitalizations in Gout, Rheumatoid Arthritis, Fibromyalgia, Osteoarthritis, and Low Back Pain

Jasvinder A. Singh[1] and John D. Cleveland[2]

ABSTRACT. ***Objective.*** To examine opioid use disorder (OUD)–related hospitalizations and associated healthcare utilization outcomes in people with 5 common musculoskeletal diseases (MSD).

Methods. We used the US National Inpatient Sample (NIS) data from 1998 to 2014 to examine the rates of OUD hospitalizations (per 100,000 NIS claims overall), time trends, and outcomes in 5 common rheumatic diseases: gout, rheumatoid arthritis (RA), fibromyalgia (FM), osteoarthritis (OA), and low back pain (LBP).

Results. OUD hospitalization rate per 100,000 total NIS claims in 1998–2000 vs 2015–2016 (and increase) were as follows: gout, 0.05 vs 1.88 (36-fold); OA, 0.68 vs 10.22 (14-fold); FM, 0.53 vs 6.98 (12-fold); RA, 0.30 vs 3.16 (9.5-fold); and LBP, 1.17 vs 7.64 (5.5-fold). The median hospital charges and hospital stays for OUD hospitalizations were as follows: gout, $18,363 and 2.5 days; RA, $17,398 and 2.4 days; FM, $15,772 and 2.1 days; OA, $16,795 and 2.4 days; and LBP, $13,722 and 2.0 days. In-hospital mortality rates ranged from 0.9% for LBP and FM to 1.7% for gout with OUD hospitalizations. Compared to those without each MSD, age-, sex-, race-, and income-adjusted total hospital charges (inflation-adjusted) for OUD hospitalizations with each rheumatic disease were as follows: gout, $697 higher; OA, $4759 lower; FM, $2082 lower; RA, $1258 lower; and LBP, $4944 lower.

Conclusion. OUD hospitalizations increased in all 5 MSD studied, but the rate of increase differed. Awareness of these OUD hospitalization trends in 5 MSD among providers, policy makers, and patients is important. Development and implementation of interventions, policies, and practices to potentially reduce OUD-associated effects in people with rheumatic diseases is needed.

Key Indexing Terms: opioid use disorder, healthcare utilization, outcomes, time trends, rheumatic diseases, musculoskeletal diseases

The opioid epidemic is a major public health crisis in the United States[1]. Opioid use disorder (OUD) has serious morbidity and mortality consequences[2,3]. OUD had a societal cost of $78.5 billion in 2013 in the US[4]. In 2017, the US Department of Health and Human Services declared OUD a public health emergency[5]; this was followed by a similar declaration by the US President[6].

Musculoskeletal diseases (MSD) are among the most common reasons for chronic pain[7] and the prescription of opioids[8,9,10,11,12]. Low back pain (LBP) is the most common MSD, followed by osteoarthritis (OA)[13]. LBP ranked the first (highest) for disability (years lived with disability)[14] and seventh for overall burden (disability-adjusted life-years) in the Global

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[1]J.A. Singh, MBBS, MPH, Medicine Service, VA Medical Center, Birmingham, and Department of Medicine at School of Medicine, and Division of Epidemiology at School of Public Health, University of Alabama at Birmingham; [2]J.D. Cleveland, MS, Department of Medicine at School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, USA.

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Address correspondence to Dr. J.A. Singh, University of Alabama at Birmingham, Faculty Office Tower 805B, 510 20th Street S, Birmingham, AL 35294-0022, USA. Email: Jasvinder.md@gmail.com.

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Burden of Disease Study 2017[15]. All MSD combined caused a significant proportion of disability in the Global Burden of Disease Study 2017[14,15]. MSD cause significant morbidity[16] and economic burden[17]. Thus, MSD constitute a major public health problem.

A recent study in multiple US clinics showed that chronic opioid use increased from 7.4% in 2002 to 16.9% in 2015 in people with rheumatoid arthritis (RA)[18]. In contrast, an older study from 1996 to 2001 showed both a low prevalence of chronic opioid use (4% or lower) and no increase in the use of opioids in older Americans with RA, LBP, or OA receiving Medicare[19]. Thus, the epidemiology of OUD in MSD is changing in parallel with the opioid epidemic in the US[1].

Due to the lack of nationally representative data, we sought to define national trends in OUD hospitalizations rates in 5 common MSD (gout, RA, fibromyalgia [FM], OA, LBP) and outcomes associated with healthcare utilization and mortality. Our study objectives were as follows: (1) examine time trends in OUD hospitalizations rates in cohorts with gout, RA, FM, OA, or LBP; and (2) compare adjusted outcomes of OUD hospitalizations between cohorts with vs without these MSD.

MATERIALS AND METHODS

Data source. We used the US National Inpatient Sample (NIS) from years 1998 to the most recent year available (i.e., 2016 to conduct this retrospective study). The US NIS is a nationally representative sample consisting of 20% of all discharges in the US[20,21]. As of 2012, the NIS contains a sample of discharge records from hospitals participating in the Healthcare Cost and Utilization Project (HCUP); there are updates from the previous data, with new definitions of hospitals and discharges being supplied by the statewide data organizations that contribute to HCUP, rather than the definitions used by the American Hospital Association Annual Survey[22]. The sampling weights of the NIS account for the correlations structure between hospital admissions by design. We used the recommended sampling weights to obtain the national estimates and used trend weights from the HCUP documentation to allow analyses across multiple years. The NIS captures all discharges regardless of the payer type. These data include characteristics of patients and hospitals, all diagnoses and procedures for hospital admission, comorbidity, and healthcare utilization. The NIS data are available publicly and contain deidentified data. The Institutional Review Board at the University of Alabama at Birmingham (UAB) approved this study and also waived the need for an informed consent for this database study with deidentified data (X120207004). All investigations were conducted in conformity with ethical principles of research. The study cohort included the US NIS from 1998 to 2016.

Study cohort and MSD of interest. We identified all OUD hospitalizations in the US NIS from 1998 to 2016 based on the presence of any of the following International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), or Tenth Revision, Clinical Modification (ICD-10-CM) diagnostic codes for opioid dependence, abuse, or poisoning in the primary diagnosis position (i.e., it was the principal diagnosis and the main reason for hospitalization) as defined by the Agency for Healthcare Research and Quality[23]: 304.0x, 304.7x, 305.5x, 965.0x, E850.0, E935.0, F111.xxx, F112.xxx, T40.1X1x–4x,T40.2X1x-4x, or T40.3X1x–4x. We excluded hospitalizations with ICD-9-CM/ICD-10-CM diagnostic or procedure codes corresponding to drug/alcohol counseling and rehabilitation/detoxification including diagnostic codes 304.03, 304.73, 305.53, F11.11xx, or F11.21xx and procedure codes 94.45, 94.64-94.69, HZ2xxxx–3xxxx, HZ4xxxx, HZ5xxxx–6xxxx, HZ81xxx–82xxx, HZ84xxx–86xxx, HZ88xxx–89xxx, HZ91xxx–92xxx, HZ94xxx–96xxx, or HZ98xxx–99xxx. This approach of identifying OUD was based on a similar approach used previously by Peterson, *et al*[24], the Centers for Disease Control and Prevention (CDC)[23], and others[25], and provided on the CDC website[26]. ICD-9-CM to ICD-10-CM coding transition was implemented in 2015 in the US and its effect on the listing of the diagnosis was minimal/none[27].

The main conditions of interest were the absence or presence of each of the 5 common MSD (rheumatic)—gout, RA, FM, OA, and LBP—due to common prevalence and their morbidity, disability, and mortality effect. We used the following validated ICD-9-CM or ICD-10-CM codes for identifying MSD in index OUD hospitalizations, listed as nonprimary diagnosis (any position after the primary DX1 position; i.e., secondary diagnoses for the hospitalization), as previously[28,29,30,31,32]: gout: 274. xx or M10.xxx; OA: 715.xx or M15.xxx–M19.xxx; RA: 714.xx or M06.xxx; FM: 729.1 or M79.7; LBP: 724.2 or M54.5. If someone had > 1 MSD condition, they were classified as having the MSD condition that appeared first among all listed secondary diagnoses.

Thus, we created 5 OUD hospitalization cohorts for each year (and also each study period), 1 for each MSD condition of interest, in order to have nonoverlapping MSD cohorts with OUD hospitalization.

Hospitalization outcomes (healthcare utilization, mortality) and covariates. We compared the following healthcare utilization outcomes following OUD admission: (1) the total hospital charges (assessed using the standard NIS variable, TOTALCHG; categorized as above or below the median); (2) discharge to home vs a rehabilitation facility (short-term hospital, skilled nursing facility, intermediate care facility, or another type of inpatient facility; using the standard NIS variable, DISPUNIFORM); and (3) the length of hospital stay (determined using the standard NIS variable, LOS; categorized as above or below the median). Total hospital charges contain the edited total charges (i.e., do not include professional fees and noncovered charges); categorizing the variable above/below the median made it relatively less susceptible to inflation-related changes over time and was similar to other previous studies[33,34]. Categorizing total hospital charges and hospital stays met the assumption for logistic regression analyses. We also assessed in-hospital mortality.

Covariates including sociodemographics (age, sex, race, income [in quartiles]), comorbidity (Deyo-Charlson comorbidity index, a validated measure that included 17 comorbidities, based on the presence of ICD-9-CM codes[35], categorized as 0, 1, and ≥ 2), insurance payer (Medicare, Medicaid, private, self-pay, or other), and hospital characteristics (hospital location/teaching status and hospital bed size) provided study cohort characteristics.

Statistical analysis. We compared unadjusted frequency (absolute number) of OUD hospitalizations from 1998 to 2016 within and between the 5 MSD cohorts. We calculated the rates of OUD hospitalizations per 100,000 NIS hospitalizations within and between the 5 MSD cohorts over time to account for secular trends in overall hospitalizations in the US over the study period. We used the chi-square test for time trends in proportion of OUD hospitalizations within each condition, further confirmed by performing logistic joinpoint regression for confirmatory analyses of change over time by using the ljr R package (version 1.4-0, R Core Team, 2016) with 1000 Monte Carlo simulations.

Rates of OUD hospitalizations were compared across age, sex, race, and income categories. We compared healthcare utilization outcomes and mortality within each MSD cohort between the first (1998–2000) and last study periods (2015–2016).

We performed multivariable-adjusted regression analyses to assess adjusted healthcare utilization or in-hospital mortality (as appropriate) by each MSD diagnosis, adjusting for age, sex, race/ethnicity, and insurance payer, to reduce confounding bias. We calculated OR and 95% CI from logistic regression analyses (nonhome discharge; hospital stay > 3 days; in-hospital mortality) and β estimates from linear regression (total hospital charges, length of hospital stay). These estimates reflected the differences in each OUD hospitalization outcome associated with the presence vs absence

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of each MSD. Sensitivity analyses were as follows: (1) adjusted only for age and sex; (2) limited the main analyses (age-, sex-, race-, and income-adjusted) to people with only 1 MSD diagnosis (i.e., excluded people with 2–5 MSD diagnoses); or (3) adjusted the main analyses multivariable-adjusted hospital charges to inflation-adjusted 2016 US dollars, using the Bureau of Labor Statistics Consumer Price Index All Urban Consumers US city average.

RESULTS

Cohort characteristics and unadjusted outcomes of OUD hospitalizations, overall. From 1998 to 2016, an estimated 781,767 OUD hospitalizations occured. The mean age was 43.7 years (standard error 0.1), 52% were male, 67% White, and 40% had a Deyo-Charlson score of one or higher. OUD hospitalizations were the highest in the lowest income classes. Approximately, 2.4% of people hospitalized primarily for OUD died during hospitalization.

Cohort characteristics of OUD hospitalizations in each MSD are provided in Table 1. The mean age was the lowest for LBP, and highest for OA and gout (Table 1). Females were predominant in the RA, FM, OA, and LBP cohorts, and males in the gout cohort. Two-thirds to three-quarters in each disease cohort were White, 25–53% had a Deyo-Charlson comorbidity score of zero (except in RA), a quarter each had Medicaid, Medicare, and private health insurance payer; most OUD hospitalizations were at urban hospitals, and a majority were at hospitals with a large bed size (Table 1).

Three-quarters of the OUD hospitalizations within each cohort were discharged to home, and the mean length of stay ranged from 3.4 days and median, 2 days for LBP to 4.3 days and median, 2.5 days for gout (Table 1). Mean/median unadjusted total hospital charges ranged from $22,794/$13,722 for LBP to $31,985/$18,363 for gout. A very small proportion of OUD hospitalizations had concomitant multiple MSD (> 1 MSD): 0.07% of the entire sample, and 10.4% of those with MSD.

Time trends in OUD hospitalizations in the 5 MSD cohorts. The absolute number of OUD hospitalizations were the highest for LBP in 1998–2000 and for OA in 2015–2016 (Table 2). Of all OUD hospitalizations in the 5 rheumatic diseases, the combined OUD hospitalizations in OA and LBP cohorts accounted for 68% in 1998–2000 and 60% in 2015–2016 (Table 2). The frequency of OUD hospitalizations was low in 1998–2000 for 5 MSD and increased over the 19-year study period (Table 2). The increase was 3.5-fold in those with LBP to 24-fold in those with gout over the study period.

Rates of OUD per 100,000 total NIS claims increased over time to 5.5-fold higher in LBP, 9.5-fold higher in RA, 12-fold higher in FM, 14-fold higher in OA, and 36-fold higher in gout (Table 2). The change in the proportion of OUD hospitalizations with a diagnosis of rheumatic disease over time was statistically significant for each of the 5 rheumatic diseases ($P < 0.0001$ each; Supplementary Table 1, available with the online version of this article), each confirmed with joinpoint regression analyses ($P < 0.0001$ each).

The rates of OUD hospitalizations per 100,000 total NIS claims over time increased for LBP, OA, and FM (Figure 1). There was a plateauing of OUD claims for LBP, FM, and gout, but the increase in rates of OUD hospitalizations continued for OA and RA (Figure 1).

Comparing 1998–2000 (the first period) to 2015–2016 (the last period), we found that most OUD hospitalization outcomes changed minimally over time in the 5 disease cohorts, except in gout. In the gout cohort, hospital charges above the median decreased from 82% in 1998–2000 to 48% in 2015–2016; length of hospital stay > 3 days decreased from 67% to 43%; and in-hospital mortality, from 9% in 1998–2000 to 2% in 2015–2016 (Table 3).

OUD hospitalizations in the 5 MSD cohorts by patient characteristics. The OUD hospitalization rates were highest for the age group > 45 to 55 years, White race, and the lowest income quartile for all 5 MSD, except in gout where Black patients had a slightly higher rate of OUD hospitalization than White patients (Table 4). Men predominated OUD hospitalizations in gout or LBP cohorts and women in RA, OA, and FM cohorts (Table 4).

By absolute numbers, age > 55 years, White race, and first and second income quartiles had the largest number of OUD hospitalizations; women outnumbered men for OUD hospitalizations in all conditions, except gout (Supplementary Table 2, available with the online version of this article).

Adjusted outcomes of OUD hospitalizations in the 5 MSD cohorts. Compared to the OUD hospitalization without each MSD, age-, sex-, race-, and income-adjusted total hospital charges (not adjusted for inflation) were as follows for each MSD: gout, $3060 higher; OA, $2180 lower; FM, $272 higher; RA, $187 higher; and LBP, $3211 lower (Table 5). The adjusted length of hospital stay and in-hospital mortality for OUD hospitalizations was significantly lower for OA, FM, and LBP vs those without each condition, respectively (Table 5).

The results were similar for sensitivity analyses, when analyses were adjusted only for age and sex (Supplementary Table 3, available with the online version of this article). Sensitivity analyses limited to only people with only 1 MSD replicated these findings with minimal numerical differences, except that the length of hospital stay and nonhome discharge were no longer significantly lower in FM (Supplementary Table 4). Sensitivity analyses that adjusted hospital charges from the main analyses to inflation-adjusted 2016 US dollar found that compared to the OUD hospitalization without each MSD, hospital charges differed as follows: gout, $697 higher; OA, $4759 lower; FM, $2082 lower; RA, $1258 lower; and LBP, $4944 lower (Supplementary Table 5).

DISCUSSION

In this national US study, we examined the OUD hospitalizations in gout, RA, FM, OA, and LBP, chosen due to their prevalence and effect on population health. Over the study period, the OUD hospitalization numbers increased by 3.5-fold in LBP and by 24-fold in gout, with lower magnitude increases in the overall OUD hospitalization rates. We noted a plateauing of OUD hospitalizations in MSD in the 3 most recent periods. Several findings merit further discussion.

The relative increase in rates of OUD hospitalizations varied

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Table 1. Characteristics for of each musculoskeletal disease cohort with OUD hospitalization[a].

	Gout, n = 1220 (n, Projected = 5980)	RA, n = 2261 (n, Projected = 11,032)	FM, n = 5309 (n, Projected = 25,893)	OA, n = 6436 (n, Projected = 31,417)	LBP, n = 7255 (n, Projected = 35,123)
Age, yrs, mean (SE); median	60.9 (0.38); 60.0	56.1 (0.30); 55.9	51.3 (0.19); 51.3	60.6 (0.18); 59.4	50.6 (0.19); 50.5
Age category, yrs					
< 34	145 (2.42)	826 (7.49)	2693 (10.40)	952 (3.03)	4964 (14.14)
34–45	596 (9.97)	1562 (14.15)	5563 (21.49)	2965 (9.44)	7609 (21.67)
> 45–55	1318 (22.05)	2883 (26.13)	7745 (29.92)	7751 (24.67)	9837 (28.01)
> 55	3920 (65.56)	5761 (52.22)	9887 (38.19)	19,749 (62.86)	12,708 (36.19)
Sex					
Male	3864 (64.62)	2271 (20.60)	2363 (9.13)	10,267 (32.68)	16,764 (47.77)
Female	2116 (35.38)	8755 (79.40)	23,514 (90.87)	21,146 (67.32)	18,331 (52.23)
Race					
White	3998 (66.87)	8072 (73.21)	19,929 (76.97)	23,248 (74.00)	25,464 (72.50)
Black	998 (16.69)	869 (7.88)	1285 (4.96)	2986 (9.50)	2071 (5.90)
Hispanic	190 (3.18)	616 (5.59)	1068 (4.13)	1206 (3.84)	1612 (4.59)
Other/missing	793 (13.26)	1469 (13.32)	3611 (13.95)	3977 (12.66)	5977 (17.02)
Deyo-Charlson Score					
0	1480 (24.75)	176 (1.60)	11,479 (44.33)	10,181 (32.41)	18,547 (52.81)
1	1280 (21.41)	4468 (40.50)	7578 (29.27)	9647 (30.70)	9079 (25.85)
≥ 2	3220 (53.84)	6388 (57.90)	6836 (26.40)	11,590 (36.89)	7497 (21.35)
Income category					
First quartile	1968 (33.55)	3294 (30.49)	7415 (29.20)	10,024 (32.64)	9665 (28.30)
Second quartile	1578 (26.91)	3001 (27.77)	7140 (28.12)	8761 (28.53)	9189 (26.91)
Third quartile	1141 (19.45)	2412 (22.33)	6407 (25.23)	6919 (22.53)	8729 (25.56)
Fourth quartile	1178 (20.08)	2098 (19.41)	4430 (17.45)	5008 (16.31)	6567 (19.23)
Insurance					
Medicaid	852 (14.28)	2061 (18.70)	5137 (19.86)	5264 (16.78)	7552 (21.54)
Medicare	3565 (59.77)	5966 (54.15)	12,044 (46.57)	18,689 (59.57)	14,327 (40.86)
Other	258 (4.33)	268 (2.44)	894 (3.46)	990 (3.15)	1910 (5.45)
Private	1036 (17.36)	2268 (20.58)	6341 (24.52)	5217 (16.63)	7970 (22.73)
Self	254 (4.25)	454 (4.12)	1446 (5.59)	1212 (3.86)	3308 (9.43)
Hospital location/teaching					
Rural	644 (10.99)	1,298 (11.97)	3467 (13.68)	4264 (13.93)	4725 (13.79)
Urban nonteaching	2139 (36.50)	4415 (40.69)	10,910 (43.05)	13,251 (43.30)	14,781 (43.15)
Urban teaching	3077 (52.51)	5136 (47.34)	10,966 (43.27)	13,087 (42.76)	14,745 (43.05)
Hospital bed size					
Small	794 (13.55)	1391 (12.82)	3498 (13.80)	4255 (13.90)	4797 (14.01)
Medium	1618 (27.61)	3118 (28.73)	6869 (27.10)	8318 (27.18)	9591 (28.00)
Large	3448 (58.83)	6341 (58.44)	14,976 (59.09)	18,030 (58.92)	19,863 (57.99)
Hospital region					
Northeast	944 (16.11)	1,529 (14.05)	3,081 (12.10)	3909 (12.71)	5138 (14.92)
Midwest	1298 (22.15)	2,502 (22.98)	6,635 (26.05)	7738 (25.15)	8241 (23.94)
South	2254 (38.46)	4,391 (40.33)	9,433 (37.04)	12,167 (39.54)	12,172 (35.36)
West	1364 (23.28)	2,466 (22.65)	6,319 (24.81)	6,956 (22.61)	8876 (25.78)
Total charges, US$, mean (SE); median	31,985 (1406); 18,363	27,696 (761); 17,398	26,147 (534); 15,772	26,639 (528); 16,795	22,794 (416); 13,722
Discharge status					
Inpatient	1427 (25.35)	2627 (25.19)	6047 (24.55)	7711 (25.71)	7090 (21.66)
Home	4203 (74.65)	7804 (74.81)	18,587 (75.45)	22,286 (74.29)	25,649 (78.34)
Length of hospital stay, days, mean (SE); median	4.3 (0.13); 2.5	3.9 (0.13); 2.4	3.7 (0.06); 2.1	3.9 (0.07); 2.4	3.4 (0.04); 2.0
Length of hospital stay category					
≤ 3 days	3709 (62.03)	7428 (67.33)	18,181 (70.22)	20,980 (66.78)	25,836 (73.56)
> 3 days	2270 (37.97)	3604 (32.67)	7712 (29.78)	10,437 (33.22)	9287 (26.44)
Died during hospitalization	104 (1.73)	171 (1.55)	220 (0.85)	325 (1.04)	314 (0.89)
Discharged against medical advice	232 (3.87)	420 (3.81)	1000 (3.86)	1052 (3.35)	2015 (5.74)

Values are expressed as n (%) unless otherwise specified. [a] OUD hospitalizations included those with the following primary diagnostic codes: 304.0x, 304.7x, 305.5x, 965.0x, E850.0, E935.0, F111.xxx, F112.xxx, T40.1X1x-4x, T40.2X1x-4x, or T40.3X1x-4x. We excluded hospitalizations with ICD-9-CM diagnostic or procedure codes corresponding to drug/alcohol counseling and rehabilitation/detoxification including diagnostic codes 304.03, 304.73, 305.53, F11.11xx, or F11.21xx and procedure codes 94.45, 94.64-94.69, HZ2xxxx–3xxxx, HZ4xxxx, HZ5xxxx–6xxxx, HZ81xxx–82xxx, HZ84xxx–86xxx, HZ88xxx–89xxx, HZ91xxx–92xxx, HZ94xxx–96xxx, HZ98xxx–99xxx. FM: fibromyalgia; ICD-9-CM: International Classification of Diseases, 9th revision, Clinical Modification; LBP: low back pain; OA: osteoarthritis; OUD: opioid use disorder; RA: rheumatoid arthritis; SE: standard error.

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Table 2. Number and rate of OUD primary hospitalizations for 5 common musculoskeletal disease cohorts from 1998 to 2016.

Year Range	OUD Hospitalizations, n				
	Gout	RA	FM	OA	LBP
1998–2000	53	314	552	702	1211
2001–2002	169	411	885	930	1753
2003–2004	247	531	1396	1558	2778
2005–2006	312	821	1488	2237	3312
2007–2008	471	1021	2461	3022	3968
2009–2010	809	1609	3997	4474	5313
2011–2012	1359	2010	5010	5494	6059
2013–2014	1220	2055	5120	5700	5275
2015–2016	1340	2260	4985	7300	5455
% change	2428	620	803	940	350

Year Range	Rate of OUD Hospitalizations per 100,000 NIS Total Claims				
	Gout	RA	FM	OA	LBP
1998–2000	0.05	0.30	0.53	0.68	1.17
2001–2002	0.23	0.57	1.22	1.28	2.41
2003–2004	0.33	0.71	1.87	2.09	3.73
2005–2006	0.41	1.08	1.96	2.95	4.36
2007–2008	0.62	1.34	3.22	3.96	5.20
2009–2010	1.08	2.14	5.32	5.96	7.08
2011–2012	1.85	2.74	6.82	7.48	8.25
2013–2014	1.72	2.90	7.22	8.03	7.43
2015–2016	1.88	3.16	6.98	10.22	7.64
% change	3568	944	1210	1409	554

FM: fibromyalgia; LBP: low back pain; NIS: National Inpatient Sample; OA: osteoarthritis; OUD: opioid use disorder; RA: rheumatoid arthritis.

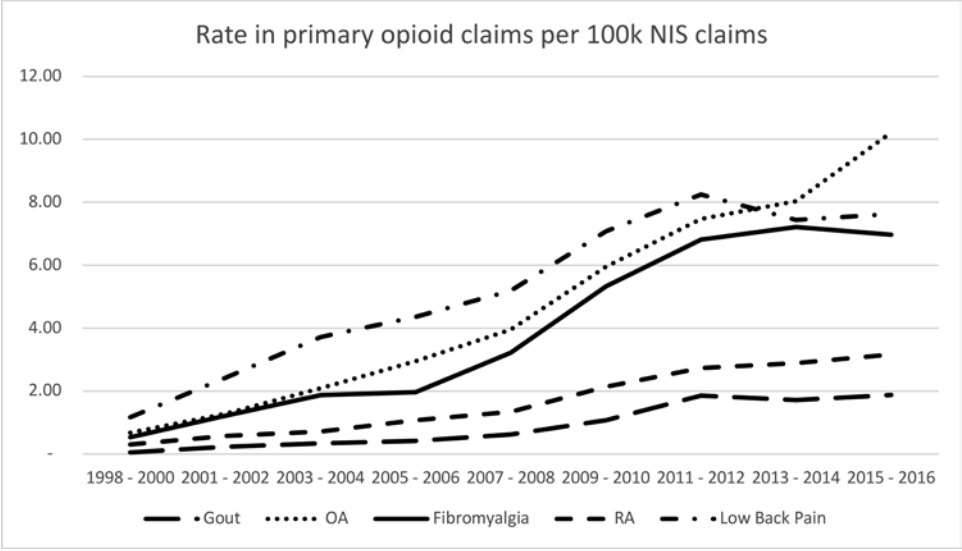

Figure 1. Trends in rates of OUD hospitalizations per 100,000 NIS claims in 5 rheumatic conditions. The X-axis represents the various study periods from 1998 to 2016. The Y-axis shows the OUD hospitalization rates per 100,000 NIS claims. NIS: National Inpatient Sample; OA: osteoarthritis; OUD: opioid use disorder; RA: rheumatoid arthritis.

across the 5 MSD (Table 2, Figure 1). To our knowledge, this is among the first studies to report national estimates for OUD hospitalization rates in gout, RA, FM, OA, and LBP. In the absence of comparative studies, these findings are of interest. We found that the actual frequency of OUD hospitalizations was low in all 5 cohorts in 1998–2000 and increased steadily over the 19-year study period. The OUD hospitalization rate varied between gout, RA, FM, OA, and LBP; it was highest for LBP at 1.2 and lowest for gout at 0.05 per 100,000 total hospitalizations in 1998–2000. In 2015–2016, the OUD hospitalization

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Table 3. Unadjusted time trends in outcomes of OUD hospitalizations for each of the 5 musculoskeletal disease cohorts.

Healthcare Utilization and Mortality Outcomes	Gout	RA	FM	OA	LBP
Total hospital charges above the median					
1998–2000	82.3	42	43	46.2	46.8
2015–2016	47.8	47.3	42.3	44.2	40.5
Nonhome discharge					
1998–2000	36.7	21.8	25.7	22.2	16.9
2015–2016	30	22.7	23.7	24.8	21.9
Length of hospital stay > 3 days					
1998–2000	67	32.3	30.7	37.9	30.8
2015–2016	42.5	35.8	37	40.5	36.6
In-hospital mortality					
1998–2000	9.3	NA[a]	0.8	0.7	2.7
2015–2016	1.9	0.7	1.6	1.1	1.1

Values are expressed in %. [a] NA since there were no deaths in the RA cohort in 1998–2000. FM: fibromyalgia; LBP: low back pain; NA: not applicable; OA: osteoarthritis; OUD: opioid use disorder; RA: rheumatoid arthritis.

rate was the highest among those with OA at 10.2 and lowest among those with gout at 1.9 per 100,000 total hospitalizations in the US. The relative increase in OUD hospitalization rates per 100,000 NIS hospitalizations over 2 decades varied from a 5.5-fold increase in the LBP cohort to 14-fold increase in the OA cohort to 36-fold increase in the gout cohort. The relative increase in OUD hospitalization rate in each of the 5 MSD far exceeds the recently reported 3.3-fold increase in the rate of overall OUD hospitalizations over the same time period in the entire US population from 59.82 per 100,000 NIS claims in 1998–2000 to 190.69 in 2015–2016[36]. This indicates that MSD cohorts may be targets for interventions for OUD hospitalizations, since a higher effect can be potentially made for OUD hospitalizations in settings with limited resources.

We found that the length of hospital stay was > 3 days for OUD hospitalization in 38%, 33%, 30%, 33%, and 26% in the gout, RA, FM, OA, and LBP cohorts, respectively. For the 5 rheumatic diseases, 22–26% of discharges were to nonhome settings. Our study provides estimates of the actual utilization burden of OUD hospitalizations in MSD cohorts.

OUD hospitalization provides a key insight into the burden and the effect of OUD in those with MSD[37]. Access to medication-assisted treatment during OUD hospitalization, inpatient addiction consultation, and coordinated postdischarge care can improve long-term outcomes of OUD hospitalization in those with MSD[37,38,39,40]. Thus, a better understanding of OUD hospitalizations can help improve our ability to end the opioid epidemic in the US in rheumatic diseases.

Data from our study need to be examined in context with what is already known about OUD in order to address the problem more effectively. Known risk factors of OUD are mental health disorders, alcohol use and problem drug use[41,42,43], prescription of opioids in general[44] and at hospital discharge[45], and duration and dose of opioid prescriptions[44]. Barriers and facilitators of chronic opioid use and opioid prescribing have been elicited[46,47], and both physician and patient perspectives on the opioid epidemic provide support for the current policies to curb prescription OUD epidemic[48,49]. These studies also provide additional insights into ways to tackle the current opioid epidemic[1,5] at patient- and system-level. OUD hospitalization offers an opportunity to initiate and coordinate addiction care, and other interventions at the individual, community, and healthcare system level can potentially improve our ability to reduce the burden and effect of OUD in those with MSD.

Age-, sex-, race-, and income-adjusted estimates and OR of OUD hospitalization outcomes differed across the 5 MSD—gout, RA, FM, OA, and LBP—when compared to the respective counterparts without each rheumatic disease. Specifically, OUD hospitalizations in gout were significantly associated with $3060 higher total hospital charges and 1.3-fold higher odds of length of hospital stay > 3 days. Hospitalization for any reason is associated with higher risk of gout flares[50], a challenging condition to treat in a person with concomitant OUD, which can prolong the hospitalization. In-hospital gout flare increased the hospital stay by 2 days in a US population-based study[50]. These outcome differences between MSD may also be due to differences in the burden of substance abuse, use of more long-acting opioids, and social determinants of health.

The study findings must be interpreted considering study limitations and strengths. The unit of analysis in NIS is hospitalization, not people. We used the diagnostic codes for the identification of the study cohort and comorbidities and, therefore, diagnostic misclassification is possible. Misclassification bias for identifying MSD and associated error rates are not available for their listing as secondary diagnosis in NIS; it should be noted that we used previously validated ICD-9-CM or ICD-10-CM diagnostic codes for identifying MSD[28,29,30,31,32]. OUD hospitalization definitions used in this study have been extensively used previously by many authors and the CDC, and are reasonably valid[23,24,25,26].

We assessed hospital charges (*a priori*–specified outcome), which are usually inflated and do not reflect the actual cost of the hospitalization. Residual confounding bias should be

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Table 4. Rates of OUD hospitalizations per 100,000 NIS claims, and absolute number of OUD hospitalizations in the first period, 1998–2000 and the last period, 2015–2016, by select patient characteristics in the 5 common musculoskeletal disease cohorts.

	Gout	RA	FM	OA	LBP
	Rates[a] of OUD hospitalizations per 100,000 NIS claims				
Age, yrs					
< 34	0.06	0.37	1.20	0.42	2.21
34–45	0.80	2.09	7.45	3.97	10.20
> 45–55	1.73	3.78	10.17	10.18	12.92
> 55	0.12	0.18	0.31	0.62	0.40
Sex					
Male	1.34	0.79	0.82	3.56	5.81
Female	0.52	2.17	5.81	5.23	4.54
Race					
White	1.05	2.13	5.25	6.12	6.71
Black	1.24	1.08	1.59	3.70	2.56
Hispanic	0.27	0.89	1.54	1.74	2.33
Other/missing	0.48	0.90	2.20	2.43	3.65
Income category					
First quartile	1.06	1.81	4.11	5.32	5.66
Second quartile	0.78	1.48	3.65	4.28	4.95
Third quartile	0.59	1.28	3.42	3.52	4.91
Fourth quartile	0.59	1.12	2.38	2.51	3.57
	No.[b] OUD Hospitalizations in 1998–2000 (First Study Period)				
Age, yrs					
< 34	Not est	Not est	80 (14.5%)	Not est	149 (12.3%)
34–45	Not est	92	247 (44.8%)	135	444 (36.7%)
> 45–55	Not est	82	148 (26.8%)	133	353 (29.2%)
> 55	Not est	125	77 (14.0%)	425	264 (21.8%)
Sex					
Male	33 (100%)	64 (20.9%)	68 (12.6%)	241 (34.4%)	634 (52.6%)
Female	Not est	244 (79.1%)	473 (87.4%)	461 (65.6%)	572 (47.4%)
Race					
White	Not est	218	371	503	887 (73.3%)
Black	Not est	Not est	38	62	57 (4.7%)
Hispanic	Not est	Not est	Not est	Not est	49 (4.0%)
Other/missing	Not est	68	128	108	217 (17.9%)
Income category					
First quartile	Not est	Not est	Not est	Not est	92 (7.8%)
Second quartile	Not est	112	168	245	404 (34.5%)
Third quartile	Not est	70	152	249	319 (27.2%)
Fourth quartile	Not est	110	203	176	358 (30.5%)
	No.[b] OUD Hospitalizations in 2015–2016 (Last Study Period)				
Age, yrs					
< 34	Not est	130 (5.8%)	510 (10.2%)	270 (3.7%)	725 (13.3%)
34–45	90	325 (14.4%)	915 (18.4%)	715 (9.8%)	840 (15.4%)
> 45–55	275	565 (25.0%)	1250 (25.1%)	1545 (21.2%)	1225 (22.5%)
> 55	945	1240 (54.9%)	2310 (46.3%)	4770 (65.3%)	2665 (48.9%)
Sex					
Male	895 (66.8%)	450 (19.9%)	495 (9.9%)	2485 (34.0%)	2540 (46.6%)
Female	445 (33.2%)	1810 (80.1%)	4490 (90.1%)	4815 (66.0%)	2915 (53.4%)
Race					
White	930	1,760 (77.9%)	4100 (82.2%)	5680 (77.8%)	4180 (76.6%)
Black	240	220 (9.7%)	275 (5.5%)	960 (13.2%)	480 (8.8%)
Hispanic	Not est	125 (5.5%)	255 (5.1%)	260 (3.6%)	300 (5.5%)
Other/missing	135	155 (6.9%)	355 (7.1%)	400 (5.5%)	495 (9.1%)
Income category					
First quartile	490 (37.3%)	790 (35.4%)	1705 (34.6%)	2645 (36.8%)	1805 (33.9%)
Second quartile	330 (25.1%)	625 (28.0%)	1290 (26.2%)	1890 (26.3%)	1260 (23.7%)
Third quartile	245 (18.6%)	470 (21.1%)	1230 (25.0%)	1595 (22.2%)	1300 (24.4%)
Fourth quartile	250 (19.0%)	345 (15.5%)	700 (14.2%)	1060 (14.7%)	955 (18.0%)

[a] Rate/100,000 claims: The numerator is frequency from Table 1 and denominator is the total NIS claims for each row category. [b] Only the number is provided without percent, since at least 1 variable category is not estimable, and an accurate percent cannot be calculated. FM: fibromyalgia; LBP: low back pain; NIS: National Inpatient Sample; Not est: not estimable since there were too few cases to create a reliable estimate; OA: osteoarthritis; OUD: opioid use disorder; RA: rheumatoid arthritis.

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Table 5. Differences in age-, sex-, race-, and income-adjusted outcomes of OUD hospitalizations by the presence of each musculoskeletal disease cohorts in regression model[a].

Adjusted Healthcare Utilization and Mortality Outcomes	Gout	RA	FM	OA	LBP
Total hospital charges, mean US$, β estimate (95% CI)[b]	**$3060 ($255–$5866)**	$187 (–1311 to 1687)	$272 (–819 to 1365)	**–$2180 (–$3287 to –$1074)**	**–$3211 (–$4091 to 2332)**
Length of hospital stay, days, mean, β estimate (95% CI)[b]	0.17 (–0.10 to 0.45)	–0.09 (–0.36 to 0.17)	**–0.17 (–0.30 to –0.05)**	**–0.16 (–0.30 to –0.02)**	**–0.47 (–0.57 to –0.38)**
Nonhome discharge, OR (95% CI)[c]	1.02 (0.88–1.17)	0.91 (0.83–1.01)	**0.86 (0.80–0.92)**	0.94 (0.88–1.00)	**0.82 (0.77–0.87)**
Hospital stay > 3 days, OR (95% CI)[c]	**1.26 (1.11–1.42)**	1.07 (0.97–1.17)	0.98 (0.92–1.05)	1.03 (0.97–1.09)	**0.87 (0.82–0.92)**
In-hospital mortality, OR (95% CI)[c]	0.71 (0.45–1.10)	0.71 (0.50–1.00)	**0.37 (0.27–0.51)**	**0.45 (0.35–0.57)**	**0.37 (0.28–0.47)**

Estimates (β estimates from linear regression and OR from logistic regression analyses) show the adjusted difference in OUD hospitalization outcomes between those with vs without each musculoskeletal condition. These regression analyses do not control for other musculoskeletal conditions. Statistically significant estimates and OR with $P < 0.05$ are in bold. P values ranged from 0.033 to < 0.0001. [a] Separate regression models were performed for each outcome within each musculoskeletal condition that adjusted for age-, sex-, race-, income-, and the presence/absence of each musculoskeletal condition; [b] linear regression for hospital charges, and hospital stay; [c] logistic regression for death, nonhome discharge and hospital stay > 3 days. FM: fibromyalgia; LBP: low back pain; OA: osteoarthritis; OUD: opioid use disorder; RA: rheumatoid arthritis.

considered while interpreting study findings, given our observational cohort study design. The estimates for the last study years (i.e., 2015 and 2016) might be affected by the coding transition from ICD-9-CM to ICD-10-CM in 2015; procedures to minimize its effect on NIS are briefly described in a publication[27]. We are unable to quantify the opioid use (type, long vs short acting, morphine mg equivalent) in our population, since data are not available in the NIS. We are unable to account for changes in management of these MSD and OUD over the past 20 years, which are important factors that can affect rates and outcomes. Lack of prehospital variables does not allow insight into discharge disposition changes over time; we suspect that changes and secular trends in covered services by insurance plans affect these time trends. We categorized people according to the MSD condition listed first among the secondary diagnoses in order to have 5 independent cohorts; however, our study does not account for people with multiple MSD. Our study was not designed to assess multiple vs single MSD diagnosis cohorts, which is an important question for future studies.

Our study has many strengths. The use of the US NIS data (i.e., a national dataset) makes the results generalizable to the US population. We adjusted estimates for several important factors, which allowed comparisons by the 5 MSD of interest. Examination of OUD hospitalization over 2 decades and associated healthcare utilization is another study strength.

In conclusion, to our knowledge, this national US study is among the first to describe the burden of OUD hospitalization in 5 common MSD: gout, RA, FM, OA, and LBP. We found a significant increase in OUD hospitalizations in MSD cohorts in the last 2 decades. A relative rate increase of 5.5-fold in LBP, 9.5-fold in RA, 12-fold in FM, 14-fold in OA, and 36-fold in gout over 2 decades provides an important insight for the OUD hospitalization burden related to MSD. Our study showed a wide range of differences in the OUD hospitalization outcomes by condition. Identification of variation in OUD hospitalization rates by age, sex, race, and income among the 5 MSD identifies some subgroups for targeted intervention. These findings can better inform patients, providers, and policy makers about the effect of OUD hospitalizations in those with common MSD, and lead to future research of interventions to reduce OUD hospitalizations in these diseases.

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ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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