

Clinical Research

# Increased Mortality and Reoperation Rates After Treatment for Septic Arthritis of the Knee in People Who Inject Drugs: Nationwide Inpatient Sample, 2000-2013

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## Abstract

**Background** The United States has a growing opioid epidemic impacting all aspects of health care including orthopaedic surgery. Septic arthritis of the knee is a condition commonly encountered by orthopaedic surgeons related to opioid and injection drug use (IDU). Changes in the frequency of hospitalizations for IDU-related septic arthritis

and differences in septic arthritis patient outcomes according to IDU status in the setting of the burgeoning opioid epidemic are unknown.

**Questions/purposes** (1) What proportion of patients with septic arthritis of the knee use injection drugs? (2) Are there any differences in complications, reoperations, length of stay, and leaving against medical advice among patients with septic arthritis of the knee with and without IDU? (3) What are the age and racial trends in IDU-related septic arthritis of the knee from 2000 to 2013?

**Methods** The Healthcare Cost and Utilization Project, Nationwide Inpatient Sample database of years 2000 to 2013 was utilized for patients between ages 15 and 64 years with a principal discharge diagnosis of native septic arthritis of the lower leg, the vast majority of which represents the knee. The Nationwide Inpatient Sample is the largest publicly available healthcare database in the United States that can show nationally representative clinical trends and outcomes. Septic arthritis was classified as related or unrelated to IDU based on previously published algorithms using billing codes. Patients with IDU-related septic arthritis were more likely to be black or Hispanic, younger, and use Medicare, Medicaid, or self-payment as their primary payment method. The yearly proportion of patients with septic arthritis who used injection drugs was determined. Hospitalization outcomes including length of stay, leaving against medical advice, number of procedures, and mortality rates were compared after adjusting for age, gender, and race in multivariable regression analyses. The yearly change in proportion of IDU-related septic arthritis in each age, race, and gender group was compared over the study period.

**Results** The proportion of patients with IDU-related septic arthritis increased from 5% in 2000 to 11% in 2013. After

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Each author certifies that his or her institution waived approval for the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.

This work was performed at Tufts University School of Medicine and Tufts Medical Center, Boston, MA, USA.

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adjusting for age, gender, and race, patients with IDU-related septic arthritis were more likely to die during hospitalization (adjusted odds ratio [AOR], 2.86; 95% confidence interval [CI], 1.51-5.39;  $p < 0.001$ ) and undergo repeat arthroscopic (AOR, 1.24; 95% CI, 1.06-1.45;  $p = 0.007$ ) or open irrigation and débridement (AOR, 1.68; 95% CI, 1.28-2.19;  $p < 0.001$ ). Patients with IDU-related septic arthritis were more likely to leave against medical advice (AOR, 7.13; 95% CI, 5.56-9.15;  $p < 0.001$ ) and also had an additional 5 days in length of stay (95% CI, 4.1-5.5;  $p < 0.001$ ) on average compared with patients with septic arthritis unrelated to IDU. There was an increasing proportion of patients with IDU-related septic arthritis who were aged 15 to 34 years and 55 to 64 years from 2000 to 2013.

**Conclusions** IDU is increasingly the cause of septic knee admissions and is associated with higher rates of mortality, reoperations, resource utilization, and leaving against medical advice. Orthopaedic surgeons must adequately screen for IDU among patients with septic arthritis and monitor them closely for reoperation with a low threshold to reaspirate a knee in the postoperative period. Future studies should determine the current use and potential benefits of a multidisciplinary approach, including addiction specialists, to aid in the management of the increasing number of these patients.

**Level of Evidence** Level III, therapeutic study.

## Introduction

Septic arthritis, the infection of one or more joints, is a condition commonly encountered by orthopaedic surgeons across all subspecialties. It is a condition associated with considerable morbidity and mortality [13] with total hospital charges at USD 759 million in the United States in 2012 [21]. High-risk populations include children, older patients, people with prosthetic joints, and people who inject drugs [6, 19]. Injection drug use (IDU)-related septic arthritis occurs either through local extension of infected skin and soft tissue near the insertion site of needles or from hematogenous seeding of joints [5, 10, 17, 18].

In light of the burgeoning opioid epidemic, trends in healthcare utilization for people with IDU-related septic arthritis is of increasing interest to the orthopaedic community [8, 16, 24]. Relative rates of complications, reoperations, and leaving against medical advice as well as the length of stay for patients diagnosed with septic arthritis with and without IDU are highly relevant but largely unknown. Intrigued by these questions, we analyzed data from a large, deidentified healthcare database with the goals of describing trends in hospital utilization for IDU-

related septic arthritis of the knee, which is the most commonly affected joint in both children and adults for bacterial and mycobacterial arthritis [22].

We therefore asked: (1) What proportion of patients hospitalized with septic arthritis of the knee are people who use drugs and how has this proportion changed over time? (2) Are there any differences in complications, reoperations, length of stay, and leaving against medical advice among patients with septic arthritis of the knee with and without IDU? (3) What are age and racial trends associated with IDU-related patients with septic arthritis of the knee from 2000 to 2013?

## Patients and Methods

### Database

We implemented a cross-sectional, comparative analysis of data from the Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Sample (NIS) database from years 2000 to 2013. The HCUP includes a variety of databases managed by the Agency for Healthcare Research and Quality (AHRQ). The NIS is the largest publicly available inpatient healthcare database in the United States with > 8 million annual inpatient observations [3]. It is a stratified systematic random sample of approximately 20% of discharges from US community hospitals (non-governmental, but including tertiary centers), excluding rehabilitation and long-term acute care hospitals. Data include diagnoses and procedural codes (International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM]), patient demographics, discharge status, demographics, and length of stay. The database has a nationally representative cohort with inclusion of a variety of hospitalization indicators, facilitating research on a broad range of topics including medical practice patterns and outcomes of treatments. Age was divided into groups 15 to 34, 35 to 54, and 55 to 64 years, whereas race was divided into six categories as reported by hospitals: white, black, Hispanic, Asian or Pacific Islander, Native American, and other.

### Classification of Septic Arthritis of the Knee

We included patients with a principal diagnosis of septic arthritis of the lower extremity (ICD-9-CM 711.06) between ages 15 and 64 years at the time of admission from January 1, 2000, to December 31, 2013. We used only a principal diagnosis code of septic arthritis of the lower extremity to maximize the precision of our case definition [11, 12]. We excluded patients with a history of arthroplasty (ICD-9-CM V43.65). Although this ICD-

9-CM code refers to the lower leg, because there is a separate ICD-9-CM code for septic arthritis of the ankle and foot (ICD-9-CM 711.07), the vast majority of these diagnoses represents septic arthritis of the knee, and throughout this article, we refer to septic arthritis of the knee.

### Classification of IDU-related Septic Arthritis of the Knee

The term IDU includes any use of illicit or nonprescription drugs. Typically, this includes opioids, cocaine, and methamphetamines. There is no validated method of which we are aware to identify people who use or inject drugs using ICD-9-CM codes. Specifically, ICD-9-CM codes do not differentiate among ways of use (eg, smoke, snort, or injection). However, several researchers have developed algorithms using ICD-9-CM codes to approximate use of drugs in patients admitted to the hospital. We used one such algorithm [25] for identifying IDU-related septic arthritis (Table 1) that seeks to identify people who use drugs based on the ICD-9-CM diagnosis codes for illicit drug use and hepatitis C virus, which are commonly present in patients with IDU. Hospitalizations were then either classified as septic arthritis of the knee related to IDU or not related to IDU.

### Patient Population

We identified 19,860 patients with a principal diagnosis of septic arthritis of the knee from 2000 to 2013, an estimate of 94,028 (95% confidence interval [CI], 90,631-97,426) patients nationwide (Table 2). In 2013 alone, there were 6995 patients with septic arthritis nationally (see Appendix, [Supplemental Digital Content](#)) for patients aged 15 to 64 years, corresponding to 3.3 patients per 100,000 person-years [23]. Overall, the median (interquartile range) age was 48 (37-56) years and 70% of hospitalizations were for male patients. Nearly 95% of hospitalizations were from patients of white, black, or Hispanic races.

Patients with IDU-related septic arthritis were more likely to be aged 35 to 54 years and less likely to be aged 55 to 64 years. A higher proportion of patients with IDU-related septic arthritis were black or Hispanic. Patients with IDU-related septic arthritis were more likely to use Medicare, Medicaid, or self-payment as their primary insurance and to have no charges for the hospitalization. Only 17% of patients with IDU-related septic arthritis used private insurance compared with 50% of people with septic arthritis unrelated to IDU (Table 2).

### Outcomes of Interest

We calculated the yearly and overall proportion of hospitalizations that were IDU-related in two populations, namely patients with septic arthritis of the knee and all patients in the NIS database from 2000 to 2013.

The main hospitalization outcomes included length of stay, total charges, the proportion of patients who left against medical advice, the proportion of patients undergoing repeat arthroscopy and arthrotomy, and mortality. For arthroscopy, we used ICD-9-CM codes 80.26, 80.46, 80.60, 80.76, 80.86, and 80.96; for arthrotomy, we used ICD-9-CM codes 80.06 and 80.16.

To compare the age and racial trends of patients with septic arthritis of the knee with and without IDU, we determined the yearly proportion of patients within each age and race category. We implemented a trend analysis of these proportions from 2000 to 2013 to determine any changes in the distribution of different age or racial groups within patients with septic arthritis with and without IDU.

### Statistical Analysis

Adjusted Wald tests were used to test for differences between patients with septic arthritis with and without IDU in demographics and hospitalization outcomes. Linear regression was used to test for trends in the proportions of various demographic groups among IDU-related septic arthritis discharges with the year of hospitalization as the independent variable. Logistic regression was used to determine the odds ratios for comparing the likelihood of leaving against medical advice, performing surgical procedures, and dying based on one's IDU status. We used multivariable analysis for both linear and logistic regressions to adjust for age, gender, and race to compute adjusted differences and adjusted odds ratios (AORs). We confirmed the goodness of fit of all logistic models using the Hosmer-Lemeshow test ( $p < 0.05$ ). Statistical significance was set at  $p < 0.05$  (two-sided). Nineteen percent of the patients were missing the race categorization, and those observations were excluded from analyses concerning race. All analyses were carried out using Stata version 12 (Stata Corp, College Station, TX, USA), and figures were produced using R 3.2.3 (R Development Core Team, Vienna, Austria). To calculate national estimates and standard errors, data were analyzed using appropriate discharge and trend weights provided by the HCUP [7]. HCUP-NIS hospital data were used to calculate appropriate standard errors when working with subsets of data only concerning patients with septic arthritis [1, 2].

Our study was exempt from the Tufts Health Sciences institutional review board because this was research not involving human subjects.

**Table 1.** ICD-9-CM diagnosis and procedure codes for identification of injection drug use

| Condition        | ICD-9-CM diagnosis code | ICD-9-CM procedure code | Diagnosis description   |  |
|------------------|-------------------------|-------------------------|---|--|
| Illicit drug use | 292.0                   |                         | Drug withdrawal   |  |
|                  | 304.00-304.03           |                         | Opioid type dependence–unspecified, continuous, episodic, in remission  |  |
|                  | 304.20-304.23           |                         | Cocaine dependence–unspecified, continuous, episodic, in remission  |  |
|                  | 304.40-304.43           |                         | Amphetamine and other psychostimulant dependence–unspecified, continuous, episodic, in remission                |  |
|                  | 304.70-304.73           |                         | Combinations of opioid type drug with any other drug dependence–unspecified, continuous, episodic, in remission |  |
|                  | 305.5                   |                         | Nondependent opioid abuse   |  |
|                  | 305.50-305.53           |                         | Opioid abuse–unspecified, continuous, episodic, in remission  |  |
|                  | 305.60-305.63           |                         | Cocaine abuse–unspecified, continuous, episodic, in remission   |  |
|                  | 305.70-305.73           |                         | Amphetamine or related acting sympathomimetic abuse–unspecified, continuous, episodic, in remission             |  |
|                  | 648.33                  |                         | Drug dependence of mother, antepartum condition or complication   |  |
|                  | 965.00                  |                         | Poisoning by opium (alkaloids), unspecified   |  |
|                  | 965.01                  |                         | Poisoning by heroin   |  |
|                  | 965.02                  |                         | Poisoning by methadone  |  |
|                  | 969.7                   |                         | Poisoning by psychostimulants   |  |
|                  | E850.0                  |                         | Accidental poisoning by heroin  |  |
|                  | E850.1                  |                         | Accidental poisoning by methadone   |  |
|                  | E854.2                  |                         | Accidental poisoning by other opiates and related narcotics   |  |
|                  |                         |                         | 94.45   | Drug addiction counseling                  |
|                  |                         |                         | 94.54   | Referral for drug addiction rehabilitation |
|                  |                         |                         | 94.64   | Drug rehabilitation                        |
|                  |                         |                         | 94.65   | Drug detoxification                        |
|                  |                         |                         | 94.66   | Drug rehabilitation and detoxification     |
|                  |                         |                         | 94.67   | Combined alcohol and drug rehabilitation   |
|                  |                         | 94.68                   | Combined alcohol and drug detoxification  |  |
|                  |                         | 94.69                   | Combined alcohol and drug rehabilitation and detoxification   |  |
| HCV              | 070.41                  |                         | Acute hepatitis C with hepatic coma   |  |
|                  | 070.44                  |                         | Chronic hepatitis C with hepatic coma   |  |
|                  | 070.51                  |                         | Acute hepatitis C without mention of hepatic coma   |  |
|                  | 070.54                  |                         | Chronic hepatitis C without mention of hepatic coma   |  |
|                  | 707.00                  |                         | Pressure ulcer, unspecified site  |  |
|                  | 707.01                  |                         | Pressure ulcer, elbow   |  |
|                  | 707.03                  |                         | Pressure ulcer, lower back  |  |
|                  | 707.10                  |                         | Ulcer of lower limb, unspecified  |  |
|                  | 707.11                  |                         | Ulcer of thigh  |  |
|                  | 707.12                  |                         | Ulcer of calf   |  |
|                  | 707.13                  |                         | Ulcer of ankle  |  |
|                  | V02.62                  |                         | Hepatitis C carrier   |  |

ICD-9-CM = International Classification of Diseases, 9<sup>th</sup> Revision, Clinical Modification; HCV = hepatitis C virus.

**Table 2.** Demographic measurements for patients with septic arthritis of the knee in the United States, stratified by injection drug use: 2000-2013 combined, Nationwide Inpatient Sample

| Indicator         | Value                     | All septic arthritis, number (%) | Septic arthritis without injection drug use, number (%) | Septic arthritis with injection drug use, number (%) | p value* |
|-------------------|---------------------------|----------------------------------|---|--|----------|
| Patients          | Total weighted number     | 94,029 (100)                     | 86,200 (92)   | 7763 (8)   |          |
| Age (years)       | 15-34                     | 19,179 (20)                      | 17,658 (21)   | 1522 (20)  | 0.426    |
|                   | 35-54                     | 48,211 (51)                      | 43,466 (50)   | 4744 (61)  | < 0.001  |
|                   | 55-64                     | 26,573 (28)                      | 25,076 (29)   | 1497 (19)  | < 0.001  |
| Sex               | Men                       | 65,519 (70)                      | 60,142 (70)   | 5476 (71)  | 0.592    |
|                   | Women                     | 28,209 (30)                      | 25,922 (30)   | 2286 (29)  | 0.592    |
| Race              | White                     | 49,324 (65)                      | 45,597 (66)   | 3723 (55)  | < 0.001  |
|                   | Black                     | 12,983 (17)                      | 11,369 (16)   | 1614 (24)  | < 0.001  |
|                   | Hispanic                  | 9613 (13)                        | 8453 (12)   | 1159 (17)  | < 0.001  |
|                   | Asian or Pacific Islander | 1204 (2)                         | 1146 (2)  | 58 (1)   | 0.005    |
|                   | Native American           | 741 (1)                          | 678 (1)   | 63 (1)   | 0.874    |
|                   | Other                     | 2226 (3)                         | 2080 (3)  | 146 (2)  | 0.115    |
| Primary insurance | Medicare                  | 14,059 (15)                      | 12,677 (15)   | 1378 (18)  | 0.005    |
|                   | Medicaid                  | 15,255 (16)                      | 12,443 (15)   | 2798 (36)  | < 0.001  |
|                   | Private insurance         | 44,727 (48)                      | 43,464 (50)   | 1329 (17)  | < 0.001  |
|                   | Self-pay                  | 9633 (10)                        | 8189 (10)   | 1440 (19)  | < 0.001  |
|                   | No charge                 | 1187 (1)                         | 1017 (1)  | 170 (2)  | 0.009    |
|                   | Other                     | 8941 (10)                        | 8304 (10)   | 628 (8)  | 0.057    |

\*Adjusted Wald test.

**Results**

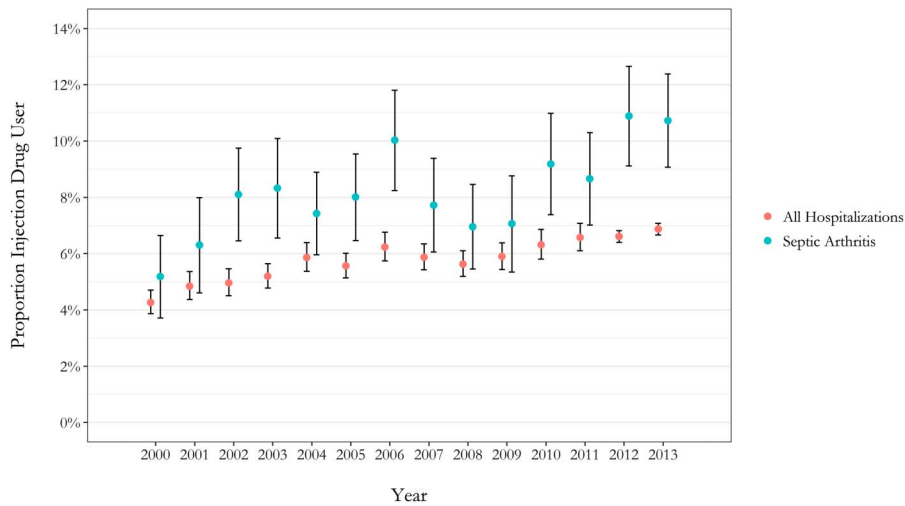
**Proportion of Patients With Septic Arthritis Related to IDU**

Over the 14 years of this study, 8% (95% CI, 7.7%-8.8%) of patients with septic arthritis of the knee had IDU-related septic arthritis (7763 patients; 95% CI, 7176-8349). From 2000 to 2013, the proportion of patients with septic arthritis who used injection drugs increased from 5% (95% CI, 3.7%-6.6%) to 11% (95% CI, 9.0%-12.3%), and the proportion of all hospitalizations that were considered IDU also increased from 4% (95% CI, 3.9%-4.7%) to approximately 7% (95% CI, 6.7%-7.1%) (Fig. 1). Over the 14 years, patients with septic arthritis had 44% higher odds of IDU (AOR, 1.44; 95% CI, 1.36-1.54) relative to all hospitalized patients within the NIS. In proportion, 8% (95% CI, 7.7%-8.8%) of patients with septic arthritis were IDU-related, whereas among all hospitalizations, nearly 6% (95% CI, 5.6%-6.0%) were IDU-related over the 14 years.

**Complications, Reoperations, Leaving Against Medical Advice, and Length of Stay**

After controlling for potential confounding variables such as age, gender, and race, we found 1.0% of patients

with septic arthritis related to IDU and 0.3% of patients with septic arthritis without IDU died during hospitalization, demonstrating that IDU was associated with higher odds of death during hospitalization (AOR, 2.86; 95% CI, 1.51-5.39; p < 0.001). After controlling for the aforementioned potential confounders, we found no difference between patients with septic arthritis with and without IDU as far as undergoing arthroscopy (AOR, 0.95; 95% CI, 0.84-1.06; p = 0.341) or arthrotomy (AOR, 1.05; 95% CI, 0.93-1.19; p = 0.428) (Table 3). However, if they had either procedure, patients with IDU-related septic arthritis were more likely to undergo a second arthroscopy (AOR, 1.24; 95% CI, 1.06-1.45; p = 0.007) or arthrotomy (AOR, 1.68; 95% CI, 1.28-2.19; p < 0.001). Patients with septic arthritis with IDU had 7.13 times the odds of leaving against medical advice relative to patients with septic arthritis without IDU (95% CI, 5.56-9.15). A total of 8% (95% CI, 6.5%-9.3%) of patients with IDU-related septic arthritis and 1.3% (95% CI, 1.1%-1.5%) of patients without IDU-related septic arthritis left against medical advice. The mean length of stay was approximately 12 days for patients with IDU-related septic arthritis compared with 7 days for patients without IDU, showing a difference on average of 5 additional days (95% CI, 4.1-5.5) (Table 4).



**Fig. 1** The proportion of patients with septic arthritis of the knee and the proportion of all hospitalized patients in the NIS classified as people who inject drugs in the United States from 2000 to 2013 is shown.

### Age and Racial Trends

Over the same time period, there was a decrease in the proportion of patients without IDU who were aged 15 to 34 and 35 to 54 years as well as an increase in the 55- to 64-year age group. Accordingly, the mean age of patients with septic arthritis without IDU increased from just under 44 years (95% CI, 40.7-46.8) in 2000 to over 47 years (95% CI, 46.5-48.0) in 2013. In contrast, among patients with IDU-related septic arthritis, there was an increase in the proportion of patients in age groups 15 to 34 and 55 to 64 years. Native Americans were the only race group that had an increase in their proportion among patients with IDU-related septic arthritis (Appendix, [Supplemental Digital Content](#)).

**Table 3.** Association of injection drug use with hospitalization outcomes among patients with septic arthritis of the knee, United States: 2000-2013, Nationwide Inpatient Sample

| Hospitalization outcome      | AOR (95% CI)*    | p value |
|------------------------------|------------------|---------|
| Left against medical advice  | 7.13 (5.56-9.15) | < 0.001 |
| Performed arthroscopy        | 0.95 (0.84-1.06) | 0.341   |
| Performed repeat arthroscopy | 1.24 (1.06-1.45) | 0.007   |
| Performed arthrotomy         | 1.05 (0.93-1.19) | 0.428   |
| Performed repeat arthrotomy  | 1.68 (1.28-2.19) | < 0.001 |
| Died                         | 2.86 (1.51-5.39) | 0.001   |

\*Multivariable logistic regression adjusted for age, sex, and race.

AOR = adjusted odds ratio; CI = confidence interval.

### Discussion

Septic arthritis is a common orthopaedic condition with considerable morbidity and mortality. This study demonstrates rising hospitalizations from IDU-related septic arthritis in the context of the opioid epidemic in terms of prevalence, complications, reoperations, mortality, and epidemiology. From 2000 to 2013, the proportion of patients with septic arthritis related to IDU more than doubled, and patients with septic arthritis with IDU had a higher likelihood of death during hospitalization, reoperations, and leaving against medical advice.

We acknowledge several limitations related to the use of a large administrative database. Our results rely on accurate coding at the hospital level, which can involve misclassifications or omissions. One such misclassification includes the categorization of race, which comes from hospital administrative records as identified by clinicians and not self-identified by patients. Although such nonrandom errors may disproportionately affect demographic distributions and hospitalization outcomes, the use of weighted results remedies these shortcomings. In regard to the NIS, its large sampling size and stratified cluster sampling methods make it a robust database that has been widely used in nationally representative studies; however, one key limitation is the inability to track individual patients through readmissions or the long-term course of their diagnosis. Furthermore, the categorization of patients as people who use drugs is subject to inaccuracies, but the use of algorithms from recent studies [25] allowed us to distinguish IDU to our best current ability. Indeed, because drug use is often underdiagnosed, we are likely underestimating the true burden of hospitalizations

**Table 4.** Hospitalization outcomes for patients with septic arthritis of the knee in the United States, stratified by injection drug use: 2000-2013 combined, Nationwide Inpatient Sample

| Hospitalization outcomes                      | Patients without injection drug use* | Patients with injection drug use* | Adjusted difference (injection drug use–no drug use) <sup>†</sup> | p value |
|---|--------------------------------------|-----------------------------------|---|---------|
| Length of stay (days)                         | 6.7 (6.5-6.8)                        | 11.5 (10.9-12.2)                  | 4.8 (4.1-5.5)   | < 0.001 |
| Left against medical advice (%)               | 1.3 (1.1-1.5)                        | 7.9 (6.5-9.3)                     | 7.1 (5.5-8.6)   | < 0.001 |
| Performed arthroscopy (%)                     | 48.7 (47.7-49.7)                     | 46.0 (43.4-48.6)                  | -1.4 (-4.2 to 1.5)  | 0.339   |
| Performed repeat arthroscopy <sup>‡</sup> (%) | 40.2 (39.0-41.4)                     | 45.1 (41.6-48.7)                  | 5.2 (1.4-9.1)   | 0.008   |
| Performed arthrotomy (%)                      | 32.0 (30.5-32.8)                     | 33.0 (30.5-35.6)                  | 1.1 (-1.7 to 3.9)   | 0.433   |
| Performed repeat arthrotomy <sup>‡</sup> (%)  | 10.5 (9.7-11.3)                      | 16.1 (12.9- 19.3)                 | 6.0 (2.4-9.6)   | 0.001   |
| Mortality (%)                                 | 0.3 (0.2-0.4)                        | 1.0 (0.5-1.4)                     | 0.6 (0.1-1.1)   | 0.021   |

\*Numbers in parentheses indicate 95% confidence intervals.

<sup>†</sup>adjusted for age, sex, and race.

<sup>‡</sup>repeat arthroscopy or arthrotomy is defined as performing greater than one arthrotomy or arthroscopy after already undergoing the respective procedure; the proportions represent the number of repeat arthroscopies or arthrotomies out of the number of patients who underwent at least one arthroscopy or arthrotomy.

from IDU-related septic arthritis. In addition, the cross-sectional study design made it difficult to quantify the relative risk of developing septic arthritis among people who use drugs or track the long-term outcomes of the patient population. Further research with prospective cohorts is needed to characterize progression of disease and long-term outcomes and to help establish temporal causality.

There could also be potential limitations associated with our multivariable regressions. Although we controlled for key demographic factors such as age, gender, and race, other factors such as socioeconomic status, homelessness, or smoking status could also have a role in the outcomes discussed. Although the NIS has potential indicators of one's socioeconomic status such as the estimated median household income for the zip code of the patient's address, including it as a covariate in our models decreased the precision of the models considerably and the CIs became quite unstable. We also considered expected primary insurance as another potential covariate, but we considered it to be (1) not necessarily a strong indicator of one's affluence; and (2) the complexity of insurance coding, especially considering the interstate differences in coding insurance status, within the NIS could introduce inaccuracies to the model. Considering these factors, we decided not to include these variables in our models. Regarding homelessness and smoking status, these are often not reflected in billing frequently and, as such, not accurate markers of true homelessness or smoking status within the NIS. These indicators would be better captured through research methods including patient interviews. Although these factors could have under- or overestimated the magnitude of certain coefficients, it is unlikely that the primary findings of this study will change considerably. Future research with more detailed patient demographic data can investigate the effect of these covariates.

We observed that a greater proportion of patients with septic arthritis also had used injectable drugs over the 14-year span of this study. The mechanism for IDU leading to septic arthritis has been well described and is likely a result of bacteria injected through nonsterile needles, bacterial contamination of drugs, or systemic spread of local cellulitis at the injection site. Bacteria then deposit in joints and lead to local inflammation and bone destruction. Because people who use drugs are more likely also to have conditions like immune deficiency and malnutrition, it is thought that they serve as vulnerable hosts who (1) fail to suppress incoming pathogens and (2) provide the space necessary for their growth, particularly in joints [20]. These mechanisms are reflected within our study showing the elevated rate of IDU among patients with septic arthritis compared with all hospitalized patients within NIS. Indeed, recent research has recognized and discussed the impact of the opioid epidemic on orthopaedic surgery as the medical specialty with the third highest opioid prescriptions in the United States [15]. Current guidelines specific for orthopaedics are sparse, but generally include better identifying patients at risk of opioid addiction, more carefully determining those truly needing opioids, and setting patient expectations for pain management and prescription administration [15].

In addition to the rising prevalence, our findings suggested that patients with IDU-related septic arthritis had a higher rate of mortality, reoperation, leaving against medical advice, and a longer length of stay relative to patients with septic arthritis without IDU. The higher likelihood of receiving greater than one arthroscopy and/or arthrotomy and a higher mortality rate both indicate that patients with IDU-related septic arthritis have a much more complex clinical management course and have a heavier burden of disease relative to patients with septic arthritis

without IDU. Higher rates of postoperative complications and reinfection for patients with IDU have been demonstrated in other pathologies associated with IDU such as infective endocarditis [9]. This is further complicated by nearly 8% of patients with IDU-related septic arthritis leaving against medical advice, which is approximately six times greater than the rate for patients without IDU and other musculoskeletal infections [14]. The risks of undertreated septic arthritis are further bone destruction, systemic spread of the infection leading to sepsis, and other more serious morbidities such as epidural abscesses and bacterial endocarditis. Based on these study results and the current lack of guidelines for treating IDU-related septic arthritis, orthopaedic surgeons should monitor patients with IDU-related septic arthritis more closely for reoperation with a low threshold to reaspirate a knee in the postoperative period as a result of the higher risk of complications and reoperations. Future studies can evaluate the effectiveness of a total synovectomy as an initial débridement in these populations and investigate the perihospital and posthospitalization courses of people with IDU-related septic arthritis, because their disease course after discharge may also markedly differ from patients without IDU.

The changing demographics of patients with IDU-related septic arthritis with an increasing proportion of younger (15–34 years of age) and older patients (55–64 years of age) need to be carefully considered in conjunction with the rising proportion of patients with septic arthritis with IDU so that these populations are adequately screened for within orthopaedic clinics treating patients with septic arthritis. These patients should also be adequately screened for in prescribing opioids for both secondary prevention and harm reduction using existing guidelines for all clinicians [4, 26].

Our results highlight the impact of the opioid epidemic on the orthopaedic patient population, specifically for patients with septic arthritis of the knee. Orthopaedic surgeons must be vigilant regarding this epidemic on two fronts, to (1) avoid aggravating the epidemic any further by prescribing opioids only when truly necessary and (2) managing patients with a history of IDU more adequately both in terms of acute treatment and long-term management. As a practice that often involves patients who go through a tremendous amount of pain, orthopaedic surgeons may find it difficult to adequately manage pain without exposing their patients to the risk of opioid addiction. Furthermore, although some guidance material for prescribing opioids exists [4, 15, 26], there is little guidance for the treatment of orthopaedic patients already dependent on opioids, who can present quite differently in the clinic as demonstrated. With the development of new guidelines, orthopaedic surgeons should receive additional training in these areas as part of their continuing medical education so that they can screen for IDU among patients with septic arthritis and treat adequately

using those guidelines. Orthopaedic surgeons should also engage in future research to evaluate the current use and potential benefits of a multidisciplinary approach, including collaboration with addiction specialists, to aid in the management of the increasing number of these patients.

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