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Approval Sheet

Modifiable Risk Factors for Complication Following Shoulder Arthroplasty: The Effect of Opioid Use, Corticosteroid Injections, and Previous Shoulder Surgery

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Abstract Cover Page

Modifiable Risk Factors for Complication Following Shoulder Arthroplasty: The Effect of Opioid Use, Corticosteroid Injections, and Previous Shoulder Surgery

By

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B.S., University of Dayton, 2015

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Abstract

Modifiable Risk Factors for Complication Following Shoulder Arthroplasty: The Effect of Opioid Use, Corticosteroid Injections, and Previous Shoulder Surgery

By Kevin X. Farley

Given an exponential increase in the utilization of primary total shoulder arthroplasty (TSA), there is an increased need for the surveillance of revision procedures and the identification of factors associated with poor postoperative outcomes. The aims of this study were to forecast the incidence and national cost of revision TSA and prosthetic joint infection (PJI) through the coming decade using the National Inpatient Sample. Subsequently, using the Truven Health MarketScan database, we aimed to identify several potentially modifiable risk factors as they relate to complication following TSA – particularly opioid use, corticosteroid injections, and a prior shoulder surgery. From 2008 to 2018, the volume of all-cause revision TSA increased 173%, while septic revision TSA increased 277%. By 2030, the estimated number of all-cause revision TSAs was projected to be 32,156, costing an estimated 738.4-millions dollars. Similarly, the estimated number of septic revision TSAs was projected to be upwards of 15,065 in 2030, costing 526.3-million dollars. We found preoperative opioid use increased complications, healthcare utilization, revision surgery, and PJI following TSA in a dose-dependent manner. The highest rate of complication was observed in those prescribed >25 oral-morphine-equivalents (OMEs) per day. These patients had an increased risk of 90-day readmission (Odds Ratio [OR]: 1.86, 95% confidence interval [CI]: 1.55-2.23), extended length of stay (OR: 2.05, CI: 1.84-2.28), a thromboembolic event (OR: 1.36, CI: 1.05-1.75), revision surgery (Hazard Ratio [HR]: 2.50, CI: 1.88-2.70), and PJI (HR: 2.80, CI: 2.25-3.49) when compared to opioid naive patients. We also found that patients receiving an injection within 30-days of surgery had an increased risk of PJI (HR: 1.67, CI: 1.21-2.32, p=0.002) compared to those not receiving an injection. No risk of PJI was seen in those receiving injections at 31-60 days (HR: 0.94, CI: 0.71-1.25) or 61-90 days (HR: 1.02, CI: 0.78-1.32) before surgery. Finally, those with a previous shoulder surgery within 4-years of their TSA had an increased risk of PJI compared to those without (HR: 1.91, CI: 1.36-2.68). We have identified three potentially modifiable risk factors for poor outcomes TSA. Care should be taken to address these risk factors preoperatively.

Cover Page

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INTRODUCTION

Hemiarthroplasty and total shoulder arthroplasty (TSA), both anatomic (1) and reverse (2), have been shown to provide significant pain relief and functional improvements (3, 4) to patients with shoulder dysfunction. As such, these procedures have increased rapidly in recent years with just over 100,000 performed in the United States (US) in 2017 alone (5). Furthermore, projections estimate 340,000 procedures being performed per year by 2025, a 235% increase (5). In accordance with this increasing incidence, the prevalence pool of patients living with shoulder arthroplasty has also markedly increased, with almost ~900,000 individuals living in the United States (US) with a shoulder prosthesis in 2017 and >2% of adults over 80 years old (6). Of note, >90% of patients living with a shoulder arthroplasty had their procedure performed in the last 10-years, likely indicating that the volume of revision procedures will continue to increase as the prevalence pool ages (6).

A variety of factors affect this recent and dramatic increase in the utilization of the total shoulder arthroplasty (TSA). These factors include an aging population, advances in prosthetic design and operative technique leading to ease of surgery and improvements in patient outcomes, and use of the reverse shoulder arthroplasty (7-11). Given this recent exponential increase in use, there is an increased need for the identification of factors associated with outcomes, complications, and resource utilization following TSA – particularly those that can be modified prior to undergoing surgery (7, 12-15).

Prosthetic joint infection is the leading cause of revision surgery for patients undergoing total knee or hip arthroplasty and is associated with significant patient morbidity, mortality, and healthcare resource utilization (16). For patients undergoing revision total hip or knee arthroplasty for septic indications, mortality is 3.7% at 90 days and 25.9% at 5-years (17), paralleling the 5-year survival rate of many other common yet morbid procedures – including kidney transplant (18), liver transplant (19), coronary artery bypass grafting (20), or elective abdominal aortic aneurysm repair (21). In addition to patient morbidity and mortality, these infections have a significant financial impact on the US healthcare system, with the cost of revision hip or knee arthroplasty for PJI totaling just under one-billion dollars in 2017 alone, and this financial impact is expected to increase to a total national cost of 1.85 billion dollars in 2030 (22).

Similar to total knee and hip arthroplasty, PJI is also one of the most serious and debilitating complications after shoulder arthroplasty, leading to implant loosening, marked shoulder dysfunction, and progressively worsening pain (23). Furthermore, PJI of the shoulder is associated with tremendous financial and resource burden on the patient and the system, with costs required to treat the infection exceeding 200% the cost of a primary arthroplasty (24). The rate of PJI after total shoulder arthroplasty is between 0.7% to 3.29% and increases to between 4% to 15.4% after aseptic revision arthroplasty (25-27).

Given the exponential increase in the utilization of the primary total shoulder arthroplasty (TSA), there is an increased need for the surveillance of revision procedures and the identification of factors associated with poor outcomes following surgery. The current national incidence of revision shoulder arthroplasty and PJI of the shoulder remain undescribed – a critical analysis to perform to allocate necessary national resources to its care. Furthermore, due to the enormous impact on patient morbidity and healthcare utilization associated with PJI of the shoulder in association with the rapidly increasing use of the total shoulder arthroplasty, it has become critical to examine factors associated with PJI following surgery. Therefore, the goal of this project is to utilize one of the largest and most comprehensive national databases available, the Truven Health MarketScan database, to identify several potentially modifiable risk factors as they relate to prosthetic joint infection, revision surgery, and complications in the shoulder arthroplasty candidate – particularly preoperative opioid use, preoperative shoulder corticosteroid injections, and a prior nonarthroplasty shoulder surgery.

BACKGROUND

The indications to perform a shoulder arthroplasty – which includes osteoarthritis, irreparable rotator cuff tears, or rotator cuff arthropathy - lead to functional limitations and chronic shoulder pain necessitating a variety of treatments before definitive management. This can include physical therapy (28, 29), corticosteroid injections (29-31), surgical rotator cuff repair (RCR) (28), glenohumeral debridement (32), or opioids (32-34). Due to the fairly elective nature of these modalities - often used to control pain or bridge the gap to definitive management (i.e., shoulder arthroplasty) - it is important to recognize if these preoperative factors effect postoperative patient outcomes.

Opioid Use

The United States has experienced an alarming increase in opioid overdoses and overdose-related deaths, spurring the Department of Health and Human Services to declare a public health emergency in 2017 (35). Contributing to the epidemic is the misuse and abuse of prescription opioids prescribed for the treatment of chronic pain. Researchers estimate that of those patients who are prescribed opioids for chronic pain, 21–29% misuse the drugs and 8–12% develop an opioid use disorder (37). Postoperative opioid prescribing may also be a nidus for abuse, with the incidence of new-onset prolonged opioid use after surgery ranging from approximately 4% to 30% (38-41).

Given these wide-ranging effects of the opioid epidemic, it is not surprising that the number of patients on preoperative narcotics undergoing procedures with pain driven indications, such as shoulder arthroplasty, is common. Approximately 25-45% of patients use opioids to manage shoulder pain prior to arthroplasty (32-34), with this wide range in prevalence likely due to physician and geographic variability in prescribing (42-45). In addition, these patients are also at an increased risk of continued and prolonged opioid use following shoulder arthroplasty (34) – potentially leading patients down a road of opioid misuse and abuse. Researchers have found similar results in anterior cruciate ligament reconstruction, total joint arthroplasty, spine surgery, and rotator cuff repair (46-53).

This high prevalence of opioid use is problematic in these populations, as preoperative opioid use has been identified as a risk factor for postoperative complication (54-58), postoperative narcotic consumption

(58), readmission (55, 56, 59) increased costs (55), and dissatisfaction (60, 61) following several orthopaedic procedures. In particular, preoperative opioid use has been found to be a predictor of revision surgery and prosthetic joint infection following total knee and hip arthroplasty (56, 59, 62-64), complications with substantial impacts on postoperative patient morbidity and healthcare utilization (16, 22). Similar studies have also identified preoperative opioid use as a negative predictor of patient-reported outcome measures (PROMs), with lower preoperative baseline scores and lower overall improvement in function following total knee or hip arthroplasty (61, 65-68). Similar relationships have also been found in patients undergoing rotator cuff repair (52, 69, 70).

The data regarding the opioid-outcome relationship in TSA, however, is primarily limited to small, single institution investigations (67, 68, 71) These studies have demonstrated that preoperative opioid use is associated with increased postoperative opioid requirements (32, 71), inferior PROMs, and increased dissatisfaction when compared to opioid naïve patients (67, 68, 72, 73). However, no studies have investigated the risk of revision surgery, prosthetic joint infection, or healthcare resource utilization. Therefore, there is a need for further investigation into the impact of preoperative opioid use in patients undergoing primary TSA using a cohort adequately powered to discern important differences.

Additionally, past studies on the opioid-outcome relationship have defined opioid use as binary (opioid users or nonusers) or by the number of opioid prescriptions received in the preoperative period (e.g., 0, 1, or >2 prescriptions). These classification systems fail to recognize the severity of opioid use and ignore the range of potential dosing based on the strength of the specific opioid type and number of tablets in the prescription (74). Oral morphine equivalents (OMEs) are able to standardize opioid doses to morphine by using a conversion factor and avoids this pitfall (i.e., 2 opioid prescription may have vastly different OMEs, yet would be considered equivalent in prior studies). Given the widespread variability in physician opioid prescribing practices and the variability of OMEs potentially contained within a single prescription (42-45), there is a need to standardize opioid use when investigating it as a risk factor.

Corticosteroid Injections

Steroid injections are easily administered and provide shoulder pain relief by suppressing local inflammation and suppressing pain-invoking cytokines (75-77). The goal of these injections is to decrease pain, improve functionality of the shoulder, and potentially delay the need for surgery. The effects of steroid injections on postoperative outcomes has been a focus for research in total knee and hip arthroplasty (78-81) and spine surgery (82-84), with prior publications revealing increased postoperative infection. Studies have shown that intra-articular injections ≤3 months before total knee arthroplasty increase the risk of prosthetic joint infection, with no increased risk if the injection is received >3 months prior to surgery (85-87). Furthermore, an increasing number of injections in the year prior to hip arthroplasty may also be associated with an even greater risk of prosthetic joint infection (88). This has led to recommendations that injections be avoided in the total hip and knee arthroplasty candidate if surgery is planned within three months. However, the impact of corticosteroids on the risk of prosthetic joint infection after shoulder arthroplasty remains ambiguous, with the only current study limited to a small cohort (89). As the use of the shoulder arthroplasty increases, elucidating the association of injections with the risk of postoperative prosthetic joint infection is of the utmost importance.

Prior Shoulder Surgery as a Risk Factor for Infection

Shoulder arthroplasty is the definitive management of many pathologies of the shoulder. However, many shoulder arthroplasty candidates, prior to their arthroplasty, receive open or arthroscopic rotator cuff repairs or arthroscopic debridement (90). During this procedure, bacterial organisms may colonize the joint space and remain in the joint asymptomatically until the time of the shoulder arthroplasty, leading to a potentially increased rate of prosthetic bacterial seeding (91). Although some of these procedures are unable to be avoided, if there is an association, it could change the management of some of these patients.

METHODS

Specific Aims

The purpose of this study was threefold. **1)** Using the National Inpatient Sample, we aimed to investigate the incidence and national cumulative costs of revision total shoulder arthroplasty in the United States, including those being performed for PJI. Using this data, we aimed to forecast the incidence and economic impact of revision shoulder arthroplasty and PJI of the shoulder in the US through the coming decade. **2)** Using the Truven Health MarketScan Database, we aimed to determine if pre-operative opioid use is correlated with increased rates of complications following shoulder arthroplasty. We hypothesized that patients prescribed higher preoperative daily averages of oral morphine equivalents (OMEs) would show increased rates of 90-day complications and long-term revision surgery following shoulder arthroplasty. We also hypothesized that a dose-dependent relationship would emerge between daily preoperative OME consumption and postoperative complications. **3)** We aimed to determine the association between preoperative opioid use, corticosteroid injections, and previous shoulder surgery on the risk of prosthetic joint infection following shoulder arthroplasty. We hypothesized that those prescribed a higher dose of preoperative OMEs, those receiving a corticosteroid injection immediately preceding arthroplasty, and those with a previous shoulder surgery would experience increased rates of postoperative prosthetic joint infection.

National Inpatient Sample

First, using the National Inpatient Sample (NIS), we sought to estimate the annual volume of revision shoulder arthroplasty and PJI of the shoulder in the US. The NIS, developed and sponsored by the Agency for Healthcare Research and Quality (AHRQ), is the largest publicly available all-payer inpatient healthcare database and was designed to produce regional and national estimates of inpatient utilization. As a 20% representative sample of all inpatient stays occurring in the United States, it can be weighted to estimate the more than 35 million hospitalizations occurring each year. The NIS has been used extensively in surgical epidemiologic research to estimate the yearly incidence of primary shoulder, hip, and knee arthroplasty in the US (7, 16, 92-97), and represents the most accurate way to estimate the national incidence of revision shoulder arthroplasty. Epidemiologic parameters for were defined as follows: *incidence* - the number of shoulder arthroplasty

procedures performed each year per 100,000 population; *procedural volume* - the gross number of procedures performed each year.

The NIS utilizes a sampling method of discharges reported by participating statewide databases to estimate all hospital discharges within the United States Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project (HCUP) (98). Using International Classification of Diseases 9th revision (ICD-9) and 10th revision (ICD-10) procedure codes, the NIS was queried from 2008 to 2018 for all patients undergoing revision shoulder arthroplasty. Those undergoing revision shoulder arthroplasty for prosthetic joint infection were identified from that initial subset using ICD-9 and ICD-10 diagnosis codes for prosthetic joint infection or using ICD-9 and ICD-10 procedure codes for implant removal and antibiotic spacer insertion. Cost for revision arthroplasty was calculated by multiplying patient total charges by hospital-specific cost-to-charge ratios (CCR) and was adjusted for inflation using the consumer price index (99). Point estimates and associated confidence intervals were calculated with discharge weights, survey stratification variables, and clustering variables provided by the NIS using the PROC SURVEYFREQ procedure in SAS. Continuous numeric variables (i.e., cost) were similarly calculated with the PROC SURVEYMEANS procedure. ICD-10 codes were utilized after October 1st, 2015, when the transition from ICD-9 to ICD-10 took place.

After yearly point estimates for incidence, volume, and cumulative national cost were obtained, independent Poisson and linear regression models were used to project the future incidence and national cumulative cost for revision shoulder arthroplasty and revision shoulder arthroplasty for PJI through 2030. The true future incidence will likely lay somewhere between these two projection models. In addition, separate Poisson and linear models were utilized to estimate the incidence among age groups and gender, as done previously (5, 16, 22, 100). All patients undergoing arthroplasty were included in the overall model. If data was missing for subgroups (missing age or gender), those patients were not included in the subgroup analysis. The Poisson and linear regression analysis were performed using the PROC REG and the PROC GENMOD (with a Poisson distribution) procedures in SAS (Version 9.4).

Truven Health MarketScan Database

Study Design

Subsequently, the Truven Health MarketScan database was then used to investigate the relationship between preoperative opioid use with short-term postoperative complications and healthcare resource utilization and the relationship between opioid use, corticosteroid injections, and a previous nonarthroplasty shoulder surgery on the risk of prosthetic joint infection. The Truven Health MarketScan Commercial Claims and Encounters and Medicare Supplemental and Coordination of Benefit databases (Truven Health, Ann Arbor, MI) is a national insurance claims database that has the distinct advantage of allowing for longitudinal follow-up of patients who remain enrolled in their insurance plan. Since 1995 the database has amassed data on 240 million patients. The data available for study included the Commercial Claims and Encounters Database, which includes insurance claims information on privately insured employees and their dependents who are covered by employer-sponsored health insurance programs, and the Medicare Supplemental and Coordination of Benefits Database, which contains claims data on retirees who are covered by Medicare Supplement insurance. Information on all facets of care is included, including inpatient hospital stays, outpatient clinical visits, health expenditures, and pharmaceutical information (101). The database also includes information regarding filled prescriptions and codes these medications using National Drug Codes (NDCs). As long as the patient remains enrolled in their insurance plan and the insurance plan remains tracked by the database, the patient can be followed longitudinally.

Patient Selection

Truven was queried from 2009 to 2018 for patients undergoing inpatient shoulder arthroplasty using Current Procedural Terminology (CPT) codes 23470 (arthroplasty, glenohumeral joint; hemiarthroplasty) or 23472 (arthroplasty, glenohumeral joint; total shoulder [glenoid and proximal humeral replacement]). We initially included all patients undergoing a shoulder arthroplasty during this time period. Patients were then excluded based on a number of criteria. We made two cohorts based on the amount of continuous preoperative insurance enrollment. Cohort 1 had at least 7-months of continuous preoperative insurance enrollment (**Figure 1A**) – to establish a baseline period to track preoperative opioid use or corticosteroid injections – and those not meeting this criteria were excluded. Cohort 2 (**Figure 1B**) had at least 4-years of continuous preoperative insurance enrollment, and those not meeting this criteria were excluded. This was done to establish a baseline

period to track a previous shoulder surgery. The other exclusion criteria between Cohort 1 and Cohort 2 were the same. First, we excluded patients who didn't have at least 90-days of continuous post-operative enrollment to ensure at least 3-months of follow up for all patients. Second, drug claims are not included for every patient, so we excluded those with no enrollment in the pharmaceutical claims database. Subsequent exclusions were done to exclude patients who may inadvertently bias our results, and these included: 1) patients >18 years old, 2) those undergoing surgery for a proximal humerus fracture or avascular necrosis, 3) those with preoperative cancer diagnoses who may be using their opioids for chronic cancer pain, and 4) those with methadone, fentanyl, or a potentially errant opioid prescription in the database. The methadone dose conversion to oral morphine equivalents uses higher OME conversion factors to account for increased methadone strength with escalating opioid doses. As such, methadone OMEs could not be reliably tracked in Truven. Secondly, fentanyl delivered though a patch delivery system could not be reliably converted to OMEs, so patients receiving fentanyl were excluded. Third, some patient had potentially errant prescriptions in the database (e.g., prescribed a 30-day supply of 900 tablets). These patients were excluded because we could not characterize if these patients were actually prescribed this amount or if this was a database error. Thus, we defined an errant pharmaceutical claim as those prescribed over 365 tablets in a single prescription, and these patients were excluded. This left 29,400 patients in cohort 1 (**Figure 1A**) and 11,211 patients in cohort 2 (**Figure 1B**).

Preoperative Patient Data

Baseline demographic, comorbid, and medication data was collected for the 6-months preceding surgery, including age, sex, comorbidities, and smoking status. The Elixhauser comorbidity index was used to classify comorbidities, and were tabulated and categorized as 0, 1, 2, 3, or 4+ comorbidities (102). Smoking status was identified through previously validated ICD-9 and ICD-10 diagnosis codes (103). The CPT code 23472, which includes both anatomic and reverse total shoulder arthroplasty under the same code, was further categorized with ICD-9 and ICD-10 codes. Patients were then categorized as having received a hemiarthroplasty, a reverse shoulder arthroplasty, or an anatomic shoulder arthroplasty with ICD-9 and ICD-10 procedure codes.

Opioid Use

We then queried the database for opioid prescriptions (hydrocodone, oxycodone, oxymorphone, dihydrocodeine morphine, hydromorphone, meperidine, and codeine) for each patient in the 7-month preoperative period using national drug codes. There is precedence for using these codes for identification of opioids in large databases (55). National drug codes used for this study were obtained from the Centers for Disease Control website (104). Tramadol or buprenorphine were not included as a preoperative opioid for the purposes of this study. Prescriptions given in the immediate month preceding surgery were not tracked as they may represent prescriptions to be used in the postoperative period. Opioid conversion tables were used to convert prescriptions into oral morphine equivalents (OME) (105). This was done by multiplying the total tablet count of the prescription by the strength of each tablet and a morphine milligram equivalent conversion factor specific to that opioid type (i.e., total tablets of prescription*tablet strength* conversion factor = total OMEs in prescription). Thereafter, we calculated average daily OMEs for each patient by dividing the total OME prescribed by the duration (in days) of the pre-operative tracking period (180 days).

Based on this data, we divided patients into the following cohorts: 1) opioid naïve (no opioid prescriptions for the 6-month preoperative period), 2) <1 OME (received an opioid prescription, but on average this was <1 OME per day), 3) 1-5 OMEs (i.e. daily average OMEs prescribed ≥1 but <5 OMEs), 4) 5-10 OMEs (i.e. daily average OMEs ≥5 OMEs but <10), 5) 10-25 OMEs (i.e. average daily OMEs were equal to or greater than 10 OMEs but <25), and 6) ≥25 OMEs (i.e. average daily OMEs were equal to or greater than 25 OMEs). As an example, for a patient averaging 5 OMEs/day, this would equate to ~200 tablets of 30-mg codeine (OME conversion factor of 0.15), ~180 tablets of 5-mg hydrocodone (OME conversion factor of 1), ~60 tablets of 10-mg oxycodone (OME conversion factor of 1.5), ~30 tablets of 10-mg oxymorphone (OME conversion factor of 3), or a combination of different opioid classes with their OMEs averaging to 5 over the 180-day preoperative time period. These classifications were chosen because they encompass a wide range of preoperative opioid use doses allowing us to widely stratify potential risk. Analysis was then subsequently performed to compare these groups.

Corticosteroid Injections

In the 3-months prior to the shoulder arthroplasty, corticosteroid injections were queried. The following CPT codes were used: 20610 (Arthrocentesis, aspiration and/or injection, major joint or bursa) and 20611 (arthrocentesis, aspiration and/or injection, major joint or bursa, ultrasound guidance). These injection codes were queried for laterality (i.e., left or right) with CPT or ICD diagnosis code laterality modifiers. Additionally, the CPT codes for injection were also linked to a shoulder related diagnosis code. These steps were done to ensure that the injection was applied to the shoulder joint and that the injection was performed on the same shoulder as the subsequent arthroplasty. Patients were then stratified into cohorts based upon the timing of their most recent injection: ≤30 days, 31-60 days, and 61-90 days prior to surgery. Healthcare Common Procedure Coding System (HCPCS) J or Q codes were further used to determine if a corticosteroid was utilized in the injection (C9469, J3300, J3301, J3302, J3303, J3304, Q9993, J1094, J1100, J0702, J1020, J1030, J1040, J2920, J2930, C9465, C9471, J7318, J7320, J7321, J7322, J7323, J7324, J7325, J7326, J7327, J7328, J7329, Q9980). The laterality of injections and of the subsequent shoulder arthroplasty were confirmed using CPT or ICD diagnosis code laterality modifiers for index shoulder arthroplasty.

Previous Shoulder Surgery

Finally, to define preoperative shoulder surgery, we used a number of arthroscopic and open shoulder related CPT codes and searched for these in the 4-year preoperative period. This included both arthroscopic (29805, 29806, 29807, 29819, 29820, 29821, 29822, 29823, 29824, 29825, 29826, 29827, 29828) and open approaches (23410, 23412, 23420, 23440, 23450, 23455, 23460, 23462, 23465, 23466). These codes included procedures such as debridement, rotator cuff repair, foreign body removal, and tendon or muscle transfers. Again, laterality was confirmed to ensure the procedure was being performed on the same joint as the subsequent arthroplasty.

Postoperative Data Collection

Complications occurring in the postoperative period were collected with the use of ICD and CPT codes and variables included with the database. First, we collected complications occurring in the 90-day period, and these included: 1) an emergency department (ED) presentation, 2) a Pain-related ED presentation, 3) 90-Day Hospital Readmission, 4) a non-home discharge destination, 5) an extended length of stay (LOS >2 days),

6) occurrence of a reoperation, 7) diagnosis of a PJI , 8) wound dehiscence, 9) the occurrent of any medical complication (including pneumonia, deep vein thrombosis, myocardial infarction, urinary tract infection, and a cerebrovascular accident [i.e. stroke]), and 10) the occurrence of a thromboembolic event. We also collected complication data for PJI and revision surgery occurring after the 90-day period – in which patients were followed from the index date to the occurrence of the outcome, end of enrollment in database, or end of the study period (end of 2018). Revision surgery was defined with CPT codes specific to revision shoulder arthroplasty (23331, 23332, 23334, 23335, 23473, 23474). To increase specificity, PJI was defined with ICD codes that had to occur on two separate physician encounter (99666, T8450, T8459).

Statistical Analysis

The opioid use cohorts were compared to opioid naive patients as the referent group (i.e., <1 OME/day compared to Opioid Naïve, 1-5 OMEs/day compared to Opioid Naïve, etc.). The injection cohorts - those receiving an injection at <30 days, 30-60 days, or 60-90 days - were compared to those not receiving an injection. Finally, those with a previous shoulder surgery were compared to those that did receive one in the 4-year preoperative period.

After allotting patients to their respective cohorts, we compared baseline characteristics and comorbidities using chi-square analysis. Furthermore, unadjusted rates of each outcome occurring in the 90-day period were compared with chi-square analysis. Thereafter, we performed binomial logistic regression to compare 90-day outcomes between groups as stated above, controlling for baseline demographic, surgical, and comorbid patient data. Survival curves were then built to look at PJI-free and revision surgery free survival times in which patients were tracked from the surgical date to the occurrence of the outcome, end of enrollment in database, or end of the study period (end of 2018). Due to low sample sizes at extremes of follow up, we only tracked outcomes for a maximum of 2500 days in Cohort 1 (**Figure 1A**) and 1000 days in Cohort 2 (**Figure 1B**). Cox proportional hazards regression was used to estimate hazard ratios (HRs) while adjusting for potential confounders. The proportional hazards assumption was tested by using time dependent covariates and comparing log-log survival curves. Extended and stratified cox models were used if the assumption was violated. Lastly, we recorded and plotted the temporal pattern of preoperative opioid prescriptions from 2009

to 2018. All statistical analysis in this study was performed using SAS version 9.4 (SAS, Cary, NC) statistical software. We defined a p-value of <0.05 to denote significance. Odds ratios (OR) or Hazard Ratios (HR) are reported with 95% confidence intervals (CI) in parentheses.

RESULTS

National Inpatient Sample

Overall Volume, Incidence, and Costs

Between 2008 and 2018, the estimated number of all-cause revision shoulder arthroplasty procedures performed per year increased from 4,066 to 11,105, a 173% increase (**Table 1**). The annual incidence per 100,000 people in the U.S. increased by 154%, from 13.37 in 2008 to 33.99 in 2018 (**Table 1**). Regarding septic revision TSA (i.e., cases being done for prosthetic joint infection), the estimated volume increased from 814 in 2008 to 3,070 in 2018, a 277% increase (**Table 1**). The incidence of septic revision arthroplasty subsequently increased from 2.68 to 9.40. Infectious indications represented 20.0% of all revision cases in 2008, which increased to 27.6% of all cases in 2018.

Table 2 demonstrates the annual procedural volume of all-cause and septic revision shoulder arthroplasty stratified by sex and age. From 2008 to 2018, all-cause revision arthroplasty increased from 1826 to 5410 in males and 2240 to 5695 in females. Over the same time period, septic revision arthroplasty increased from 454 to 1795 in males and 360 to 1275 in females. There was also growth in all age and sex subgroups (**Table 2**). With age and sex stratification, the largest overall growth for all-cause revision arthroplasty was seen in males and females aged 65-74 years old, with an increase of 273% and 203%, respectively. Likewise, for septic revision arthroplasty, the largest overall growth was seen in males 65-74 years old, with an increase of 459%, and females aged 55-64 years old, with an increase of 340%. Although females were 51% of the all-cause revision TSA cohort, they only represented 42% of those undergoing surgery for septic indications.

Table 3 displays the average cost per revision and the national cumulative cost of revisions per year. The average cost for all-cause revision arthroplasty increased 5% from 2008 to 2018. Likewise, the average cost per septic revision arthroplasty increased 29% over the same time period. The yearly national cumulative cost for all-cause revision arthroplasty increased from 74 million dollars in 2008 to 226 million dollars in 2018, a 203% increase. Likewise, the national cumulative cost associated with septic revision shoulder arthroplasty increased from 14 million dollars in 2008 to 73 million dollars in 2018, a 406% increase.

Projections to 2030

Linear and Poisson regression analyses demonstrated significant increases in the volume of all-cause and septic revision shoulder arthroplasty from 2018 to 2030 (**Table 4).** By 2030, the linear model predicts that the volume of all-cause revision arthroplasty will increase to 18,381 cases/year, a 65% increase. According to the Poisson model, the projected volume will increase to 32,156 procedures, a 189% increase. The projections for septic revision TSA demonstrated even more substantial increases, with projected volume increases by the linear and Poisson models of 78% and 391%, to an estimated 5,466 and 15,065 procedures, respectively. The national cumulative cost of all-cause revision TSA was expected to rise dramatically, increasing to 381 million dollars and 738 million dollars by the linear and Poisson models, respectively (**Figure 2**). Septic revision shoulder arthroplasty was expected to have a cumulative cost burden of 134 million dollars and 526 million dollars, by the linear and Poisson models, respectively (**Figure 3**).

Truven Health MarketScan Database

From 2009 to 2018, using the Truven database, we identified 29,400 patients with 7-month continuous preoperative enrollment and 11,211 patients with 4-year preoperative enrollment meeting our inclusion and exclusion criteria (**Figure 1**). We separated these patients into the opioid use, injection, and previous shoulder surgery cohorts as described above.

Opioid Use

Baseline Patient Differences in Opioid Use Groups

From 2009 to 2018, we identified a total of 12,660 (43%) patients who were using opioids in the preoperative period. The distribution of patients among the OME groups is displayed in **Table 5**. The majority (57%) of patients were opioid-naïve, with the next most common group receiving 1-5 OMEs/day (16%). 2,487 (8.5%) patients were in our highest opioid use group (>25 OMEs/day on average). Chi-square analysis revealed that there were multiple baseline differences between cohorts. While differences were often small, they were universally higher in patients prescribed a higher number of OMEs. Patients on preoperative opioids tended to be younger on average, with an average age of 63.5 years in those prescribed >25 OME/day and 66.9 years in the opioid naïve group. Additionally, in opioid use cohorts prescribed a larger amount, there was a higher

proportion of females, a higher proportion of patients with 4 or more Elixhauser comorbidities, and a higher rate of tobacco use (**Table 5**).

Ninety Day Complications in Opioid Use Groups

Ninety-day complication data was compared between opioid use groups and is displayed in **Table 6** and **Table 7**. Univariate analysis revealed that there were significant differences between groups in every examined outcome. With very few exceptions, the gross rate of occurrence for each complication increased with increasing preoperative opioid consumption (**Table 6)**. Subsequently, we performed multivariate analysis to control for potential confounding, and confirmed many of the differences revealed by our univariate model (**Table 7**). The rates of postoperative ED presentation increased from 9% in opioid naïve patients to 13% in those taking >25 OMEs per day. This equated to a 1.48 (1.30-1.68) times increased odds of ED presentation in patients taking >25 OMEs per day compared to opioid naïve patients. Pain related visits to the emergency department also increased – with only 0.65% of opioid naïve patients visiting the ED for a pain related diagnosis compared to 2.1% of those taking >25 OMEs per day. This equated to a 2.22 (CI: 1.59-3.11) times increased odds in the >25 OME group compared to the opioid naïve group. 90-day readmission also exhibited the same trend, increasing 3.3% to 7% from opioid naïve to the 25-OME cohort, which was roughly a 1.86 (CI: 1.55-2.23) times increased odds of ED presentation compared to opioid naïve patients. Similar trends were also seen for non-home discharge destination and an extended hospital length of stay.

Furthermore, we saw those patients taking >25 OMEs had a 90-day reoperation rate of 3.62% compared to a rate of 1.6% in the opioid naive patients, equating to a 2.27 (CI: 1.76-2.93) times increased odds of revision surgery. While the other opioid groups had higher rates of reoperation, there wasn't a clear trend between them (**Table 7**). Rates of 90-day prosthetic joint infection were only significantly increased in the 10-25 (OR: 2.33, CI: 1.46-3.71) and >25 OME (OR: 2.76, CI: 1.85-4.12) groups compared to opioid naïve patients. Increased rates of venous thromboembolism were only seen in the opioid use group taking >25 OME (OR: 1.36, CI: 1.05-1.75).

Survival Analysis of Infection and Revision in Opioid Use Groups

Survival analysis revealed that opioid-use groups generally had an increased risk of PJI (**Table 8**) and revision surgery (**Table 9**) when tracked past the 90-day postoperative period. Rates of PJI/100-patient years increased from 0.69 in opioid naïve patients to 2.1 in those taking >25 OMEs per day. Likewise, rates of revision surgery/100-patient years increased from 1.15 in opioid naive patients to 2.89 in those taking >25 OMEs per day. On extended cox modeling, while adjusting for covariates, we found that groups consuming >25 OMEs/day (HR: 2.80, CI: 2.26-3.49), 10-25 OMEs/day (HR: 1.93, CI: 1.48-2.53), and 5-10 OMEs/day (HR: 2.01, CI: 1.54-2.63) had the highest risk of developing a prosthetic joint infection when compared to opioid naïve patients (**Table 8**). Similarly, the >25 OMEs/day (HR: 2.25, CI: 1.88-2.71) and 10-25 OMEs/day (HR: 1.61, CI: 1.28-2.02) groups had the highest risk of needing to undergo revision surgery (**Table 9**).

Trends in Preoperative Opioid Use

From 2009 to 2018, the proportion of opioid-naïve patients increased nearly every year from ~52% in 2009 to just over 65% in 2018. Concurrently, the three highest opioid use cohorts in this group decreased over the same period. The lowest OME cohort (<1 OME/day) stayed level over the time period (**Figure 4**).

Preoperative Injections

The distribution of patients among the injection cohorts is displayed **Table 10**. The majority of patients did not receive an injection within 90-days of surgery (79.60%), while 3.07% received an injection within 30-days of surgery, 7.93% received an injection 31-60 days before surgery, and 9.38% patients received an injection 61-90 days before surgery. In general, patients receiving injections, especially those receiving one within 30 days of surgery, tended to be female, have a higher number of comorbidities, use opioids, and be undergoing a reverse shoulder arthroplasty (**Table 10**).

The univariate and multivariate analysis of 90-day PJI between injection groups is displayed in **Table 11**. The <30-day injection group had an unadjusted PJI rate of 1.11%, compared to 0.69% in the injection-naïve group (p=0.140). This difference was not statistically significant on multivariate analysis (OR: 1.42, CI: 0.74-2.70, p-value: 0.293). On univariate or multivariate analysis, there was also no difference in the 31–60-day injection group (OR: 0.57, CI: 0.30-1.09, p=0.091) or the 61–90-day injection group (OR: 0.86, CI: 0.52-1.43, p=0.561) when compared to the injection naïve group.

However, survival analysis revealed differences in the rates of longer-term prosthetic joint infection (**Table 12**). Rates of PJI/100-patient years in those receiving an injection <30 days prior to surgery was 1.74 compared to 0.92 in the injection naïve group ($p<0.001$), revealing an unadjusted HR of 1.89 (CI: 1.37-2.63) in the <30-day injection cohort compared to the injection-naïve group. On extended cox modeling, while adjusting for covariates, this relationship was confirmed for <30-day injection group (HR: 1.67, CI: 1.21-2.32, $p=0.002$). There was no difference seen for the 31–60-day injection group (HR: 0.95, CI: 0.71-1.25, $p=0.700$) or the 61–90-day injection group (HR: 1.03, CI: 0.79-1.33, $p=0.852$) when compared to injection naïve patients.

Previous Nonarthroplasty Shoulder Surgery

We found that 14.9% of patients had undergone a previous shoulder surgery in the 4-years preceding arthroplasty. Patients with previous surgery tended to be younger, female, use opioids, and be undergoing a reverse. There were only minor differences in comorbidity burden, tobacco use, or preoperative injections (**Table 13**). We saw a 0.42% 90-day rate of PJI in those without a previous shoulder surgery vs. 1.38% in those with a previous surgery – which equated to a 2.75 (CI: 1.59-4.76, $p<0.001$) times increased odds of PJI (**Table 14**). Rates of PJI/100-patient years in those receiving a previous shoulder was 1.56 compared to 0.65 in those without a previous shoulder surgery ($p<0.001$). This revealed an unadjusted HR of 1.91 (CIL 1.36-2.68, $p<0.001$) between the groups. These findings were further verified on cox proportional hazards regression, where a 2.99 (CI: 1.84-4.85, $p<0.001$) times increased hazard of PJI in those receiving a previous shoulder surgery compared to those without a previous shoulder surgery (**Table 15**).

DISCUSSION

Given the recent and dramatic rise in utilization of the TSA in the US, there is an increased need for the identification of factors associated with outcomes, complications, and resource utilization following surgery – particularly those that can be modified preoperatively (7, 12-15). In the current study, we found several potentially modifiable risk factors for deleterious outcomes following shoulder arthroplasty. Patients on preoperative opioids had a higher rate of complications in the 90-day period following shoulder arthroplasty. These complications were seen at subsequently higher rates in those taking a greater amount of OMEs, meaning that the relationship may be partially dose dependent. Furthermore, although preoperative opioid use was common in this study (43% of all patients), its frequency seemed to be decreasing over the study period – possibly indicating that efforts to combat the opioid epidemic have been effective. Patients taking >25 OMEs had the highest risk of PJI, but increased risk was still present in those taking 5-10 and 10-25 OMEs per day. Likewise, we found that corticosteroid injections were associated with an increased risk of PJI if given within 30-days of surgery, but not if given at other time points. Similarly, patients with a previous shoulder surgery also showed increased rates of PJI. Finally, we found that the national incidence of revision shoulder arthroplasty is increasing and may impose a significant burden on the US healthcare system in the coming years. This is especially true regarding revision surgery being done for prosthetic joint infection, where there will be a possible 15,000 septic revision surgeries being performed in 2030, costing the US healthcare system 500-million dollars.

Opioid Use

The opioid epidemic has emerged as one of the most important public health issues in the US (106). Despite evidence and recommendations directly contradicting the practice (107), there are a high number of patients with chronic pain being managed with chronic opiates. This is contributing to the large number of patients undergoing procedures with pain-related indications, such as total joint arthroplasty, that are on preoperative opioids (108). Further complicating matters is that many of these preoperative prescriptions are not from orthopedic surgeons (109). As the patient on preoperative opioids is frequently encountered, the impact that opioids have on postoperative outcomes is critical to understand.

The results of this study indicate that preoperative opioid use prior to TSA is common and present in ~43% of patients. This represents a concerning finding, given the implications that preoperative opioid use has on outcomes following TSA. We found that preoperative opioid use increased complications, perioperative healthcare utilization and costs, revision surgery, and prosthetic joint infection following TSA. This relationship was dose-dependent – i.e., those taking a greater amount had a greater risk of developing a complication. This dose-dependent response was robust and, as such, reducing opioid use prior to TSA may diminish the deleterious effects it has on postoperative outcomes. This is especially true in those in those opioid-use groups averaging >10 OMEs/day. Nevertheless, the decreasing incidence of preoperative opioid use over the study period (~10% total reduction in preoperative opioid users from 2009 to 2018) is reassuring and suggests that physicians are already taking action in lieu of a growing epidemic.

Our findings are consistent with those in lower extremity arthroplasty, which has shown higher rates of infection (54), revision surgery (59, 110, 111), and readmissions (59) in those on preoperative opioids seeking surgery. We further found an increased rate of overall and pain related presentations to the ED, as well as medical and surgical complications, such as thromboembolism, in those on preoperative opioids. The reason for these associations is multifactorial. Patients on opioids require greater postoperative analgesics secondary to opioid sensitization and poor pain control (51-53, 112, 113), possibly leading to increased rates of dissatisfaction with surgery (114, 115). This is seen in prior literature, where those on preoperative opioids undergoing orthopaedic surgery have lower baseline patient reported outcome measures that subsequently fail to increase as much as their opioid-naïve counterparts following surgery (61, 65-69, 116). Dissatisfaction with surgery, poor pain control, and a poor response to surgery likely drives the increased rates of hospital admissions, ED presentations, and revision surgery seen in those taking preoperative opioids.

Furthermore, opioids have been associated with delayed wound healing (117) and immune cell impairment (118) – which can lead to an increased risk of postoperative infection. This was demonstrated in our study by a 2-times increased risk of PJI in those taking >10 OMEs/day prior to surgery. This also explains the increased risk of medical complications - including pneumonia and urinary tract infection - in those on preoperative opioids. Additionally, while basic science studies have shown that opioids may prevent platelet

aggregation (119), opioids have been shown clinically to be associated with an increased risk of thromboembolic events following various orthopedic procedures (120-122). It has been suggested that that this is a result of abnormal hematological parameters in those on opioids, such as increased fibrinogen and c-reactive protein (CRP), which increases the risk of thromboembolism (123, 124). Additionally, those patients requiring high doses of opioids are less likely to be ambulatory immediately following surgery - further intensifying this association. This relationship was highlighted in our study with a 2-times increased risk of 90-day thromboembolism in patients prescribed >25 OMEs/day.

Nevertheless, given the high-complication profile of patients on preoperative opioids, it is reassuring that preoperative opioid use decreased over the study period. From 2009 to 2018, the OME cohorts with the highest rates of detrimental postoperative outcomes – those taking 5–10 OMEs, 10-25 OMEs, and >25 OMEs/day – decreased in frequency from 2009 to 2018. This is likely secondary to a response by the medical community to combat the opioid epidemic through guideline-directed prescribing for chronic pain, as recommended by the Centers for Disease Control (125-127). Furthermore, orthopaedic governing bodies have further made directives dissuading the use of opioids for the management of joint arthritis (107, 125-127). Finally, mandates enforcing required checks of statewide prescription monitoring programs prior to prescribing an opiate or legislation aimed at combatting excessive prescriptions through limits on OMEs may be further driving reductions in opioid use (125, 128-130).

Corticosteroids

Studies have investigated the association between steroid injections and postoperative complications in numerous orthopaedic surgical procedures (78-83). Specific to TSA, prior studies investigating the injection-outcome relationship have been limited by small sample-sizes. The only available study is underpowered with only 23 patients in the injection cohort and 1 prosthetic joint infection event in the entire study (89). Our findings, adequately powered with a total sample size of 29,400, suggest that injections received within 30-days of a TSA are associated with an increased risk of PJI following surgery. This association was not seen if the injection was given at 31-60 days or 61-90 days, suggesting that injections given outside of the 30-day preoperative window can be safely given to patients.

These results expand upon those of prior investigations which have shown therapeutic corticosteroid injections to be a modifiable risk factor for prosthetic joint infection following total joint arthroplasty (79, 87, 131, 132), infection and revision following rotator cuff repair (78, 80, 133), and infection following hip arthroscopy (81). Our findings strengthen the body of evidence that suggests corticosteroids increase the risk of infection if given within a short time frame of operative intervention (134), which has led to recommendations for their complete cessation if total knee or hip arthroplasty is planned within 3-months (134). Based on our data, we recommend the complete cessation of injections within 30-days of shoulder arthroplasty, and patients should be counseled on this increased risk if they are required.

There are several mechanisms that may be driving the injection-infection relationship. Increased rates of infection may be secondary to the local immunosuppressant effects of the corticosteroid at the injection site – in addition to breaking the skin barrier prior to surgery – which may potentially seed the area and predispose to prosthetic infection (135-138). Likewise, corticosteroids have also been shown to lower tissue deposition of important wound healing growth factors, which may predispose to wound complications (138).

Projections of Revision Shoulder Arthroplasty

From the years 2008 to 2018, all-cause revision shoulder arthroplasty volume increased by ~173%, while septic revision shoulder arthroplasty increased 277%. The greatest increases were seen in male and female subgroups aged 55-74 years old. By 2030, the estimated number of all-cause revision TSAs was projected to be ~32,000 in 2030, with an estimated cumulative national cost burden of 750-millions dollars in 2030. Similarly, the estimated number of septic revision TSAs was projected to be upwards of ~15,000 cases in 2030, with a possible total cost burden upwards of 500-million dollars.

These findings are mirrored by those in the total knee and hip arthroplasty literature, where there is a projected 1.85-billion-dollar cost burden associated with septic revision total hip and knee arthroplasty in 2030 – primarily driven by large increases in procedural volume (22). The increases in revision shoulder arthroplasty seen in this analysis is driven by a recent and rapid rise in the utilization of the primary TSA, with >100,000 procedures being performed in 2017 alone (5). Furthermore, projections estimate 340,000 primary procedures being performed per year by 2025, a 235% increase (5). When analyzing the prevalence of TSA, >90% of

patients living with a shoulder arthroplasty had their procedure performed in the last 10-years, and 65% within the last 5-years (6). This indicates that the volume of revision procedures will continue to rise, especially as the prevalence pool ages.

While reasonable outcomes after revision surgery can be achieved and while the reverse TSA has made revision procedures technically less challenging than revision anatomic TSA (139-142), revision options in shoulder arthroplasty are somewhat limited in comparison with hip and knee arthroplasty, creating an ongoing need for technical and technological progress. These are all important considerations as these procedural volumes increase (15, 142, 143). Some hopeful considerations include that the stemless shoulder arthroplasty has equivalent mid-term data available compared to stemmed arthroplasty, which has the benefit of bone preservation, thus, potentially decreasing revision morbidity – and potentially decreasing the cost analysis projections seen in this study (144-146).

Furthermore, surveillance of the growing number of revision procedures in the US raises questions regarding health care resources. As the number of revision procedures increases, there will be an increased demand for adequately trained orthopaedic surgeons specialized in revision shoulder arthroplasty. In ABOS (American Board of Orthopaedic Surgery) Part II candidates (board-eligible surgeons who must submit 6 consecutive months of clinical cases in order to be board certified), the majority of primary TSAs from 2010-2017 were performed by non-shoulder fellowship trained surgeons (148). Likewise, only ~100 ABOS Part II candidates specializing in shoulder surgery performed primary arthroplasty over the same time period, indicating there may be a relative shortage of surgeons optimally trained and comfortable with managing this increasing revision demand. Furthermore, the number of shoulder and elbow fellowship spots has not responded to the growing demand, remaining stable over the past several years (149). The need for adequately trained surgeons will need to be met over the next decade, either through increasing the number of fellowship trained shoulder surgeons or increased training in revision shoulder arthroplasty throughout orthopaedic surgery residency.

Strengths and Limitations

There are multiple limitations to this investigation. First, we are reliant on accurate coding for proper patient identification as well as reporting of postoperative complications, which is inherent to the analysis of any large database. Another important set of limitations deals with the inability to validate the accuracy of future projections. There are many drivers of procedural growth, some of which we cannot predict. New technological innovations in primary arthroplasty may mitigate the need for revision surgery or the cost of revision procedures. Additionally, due to limitations in the NIS, we were not able to estimate the incidence of shoulder arthroplasty by implant characteristic, and this should be the focus of future work.

Next, we were reliant on national drug codes to identify preoperative opioid prescriptions. However, there is significant precedence in the literature for this (59, 61, 150, 151). Furthermore, different opioid classes were not considered individually in this study, and there could be differences between them. We controlled for this by converting opioid prescriptions into OMEs – which is a more reliable indicator of actual opioid use then categorizing opioid use with a binary classification or by prescription count, as past studies have done.

Some factors that have been demonstrated to influence outcomes were not available for analysis and could not be analyzed. These include hospital and surgeon volume (152-154) and case complexity as dictated by anatomical factors (i.e., glenoid bone loss, bone quality, etc.). We attempted to remove some of these possible biases by excluding patients undergoing surgery for fracture, excluding those with an avascular necrosis diagnosis, and including shoulder arthroplasty type as a covariate when computing adjusted odds and hazard ratios. Similarly, there were baseline differences between cohorts, and while we controlled for these statistically, the potential exists that these differences could bias our results. Additionally, while our analysis controlled for many available factors, it must be acknowledged that many of our examined outcomes of interest have multifactorial influences. The associations found in this study might be a surrogate for other confounding variables that are associated with opioid use, injections, or a previous surgery. For example, our finding of increased revision surgery in those on opioids might be a product of poor pain control or satisfaction associated with chronic opioid usage. Finally, the association between hospital admissions and complications might be explained by an association of increased comorbidities in those on preoperative opioids that was not adequately controlled for on our multivariable analyses. These limitations are important to recognize and consider.

Finally, the Truven MarketScan database contains information only on patients with private, employee sponsored medical insurance or those with Medicare supplemental insurance. Uninsured patients, those with other private insurance plans not included by the MarketScan database, those with Medicare advantage, and those with Medicaid would not be included in this analysis, potentially limiting the generalizability to these specific patient cohorts.

Despite these limitations, the databases used in this study represent a strength. The NIS database represents the best available database to analyze national trends irrespective of payer status and has been used extensively for this purpose (10, 12, 92-94, 155-160). The Truven MarketScan database represents a strength of the current investigation when examining modifiable risk factors for complications. The database allows for analysis of a large number of patients, includes information from both inpatient and outpatient domains, includes pharmaceutical drug claims, and allows for longitudinal follow-up of patients as long as they remain enrolled in their healthcare plan. This allowed us to track 29,400 patients for as far as 2500 days postoperatively – overcoming the deficiencies of past studies when analyzing the opioid-outcome and injection-outcome relationship. Additionally, this is much more than the 30-90 days of follow up allowed by other databases (161).

Conclusion

In conclusion, preoperative opioid use is a risk factor for complication, increased healthcare utilization, and revision surgery following TSA. This risk occurs in a dose-dependent manner. Encouragingly, providers have already started to trend in the right direction with preoperative opioid prescription patterns, but more work remains as approximately 40% of patients in our cohort continued to receive preoperative opioids in 2018. Surgeons should counsel at-risk patients regarding their increased risk prior to surgery, and opioid reduction strategies should be discussed by both patients and providers, including making efforts to cut opioid use to <10 OMEs per day (with an ultimate goal of complete cessation) in order to reduce the number of patients in the highest-risk groups. Furthermore, this study comprises an important contribution to the understanding of risk in relation to timing between steroid injections and TSA – suggesting that these injections should be held if surgery is planned within 30 days. Our hope is that the findings of this study will allow providers to inform patients on the risks and benefits of a corticosteroid injection and surgery. Furthermore,

our study also clearly demonstrates the large economic and clinical burden that revision shoulder arthroplasty will have on orthopaedic providers and the US healthcare system. This information should be used to allocate the necessary national resources to its care.

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TABLES

Table 1. Revision Shoulder Arthroplasty Volume and Incidence, 2008-2018

Year	All Cause Revision Shoulder Arthroplasty		Septic Revision Shoulder Arthroplasty	
	Volume	Incidence	Volume	Incidence
2008	4066 (3473-4659)	13.37 (11.42-15.32)	814 (715-912)	2.68 (2.35-3)
2009	5171 (4190-6153)	16.86 (13.66-20.06)	866 (682-1051)	2.82 (2.22-3.43)
2010	6204 (5004-7404)	20.06 (16.18-23.94)	1363 (1035-1691)	4.41 (3.35-5.47)
2011	6220 (5256-7185)	19.96 (16.87-23.06)	1194 (976-1412)	3.83 (3.13-4.53)
2012	6240 (5728-6752)	19.88 (18.25-21.51)	1350 (1244-1456)	4.3 (3.96-4.64)
2013	6780 (6318-7242)	21.46 (19.99-22.92)	1480 (1382-1578)	4.68 (4.37-4.99)
2014	7310 (6786-7834)	22.97 (21.32-24.61)	1475 (1343-1607)	4.63 (4.22-5.05)
2015	8520 (7965-9075)	26.57 (24.84-28.3)	1885 (1760-2010)	5.88 (5.49-6.27)
2016	9475 (8871-10079)	29.34 (27.47-31.21)	2625 (2419-2831)	8.13 (7.49-8.77)
2017	10270 (9601-10939)	31.6 (29.54-33.66)	2785 (2582-2988)	8.57 (7.94-9.19)
2018	11105 (10428-11782)	33.99 (31.92-36.07)	3070 (2855-3285)	9.4 (8.74-10.06)
Percent Change	173%	154%	277%	251%

* 95% Confidence Intervals in Parantheses; Incidence represented as per 100,000 population

Table 2. Volume of all-cause and septic revision shoulder arthroplasty by age and sex, 2008-2018

Year		All Cause Revision Shoulder Arthroplasty			Septic Revision Shoulder Arthroplasty		
		2008	2018	% Change	2011	2017	% Change
Male	45-54 yr	265 (167-363)	455 (361-549)	72%	51 (14-88)	180 (122-238)	252%
	55-64 yr	560 (436-684)	1605 (1403-1807)	187%	157 (109-205)	560 (456-664)	256%
	65-74 yr	561 (421-701)	2095 (1865-2325)	273%	135 (83-187)	755 (631-879)	459%
	≥75 yr	321 (230-413)	1115 (968-1262)	247%	85 (49-121)	240 (181-299)	182%
	Total	1826 (1513-2139)	5410 (4981-5839)	196%	454 (364-543)	1795 (1609-1981)	295%
Female	45-54 yr	194 (123-266)	355 (268-442)	83%	24 (3-46)	90 (47-133)	275%
	55-64 yr	541 (404-679)	1490 (1314-1666)	175%	84 (43-124)	370 (296-444)	340%
	65-74 yr	757 (582-932)	2295 (2071-2519)	203%	112 (58-167)	470 (380-560)	317%
	≥75 yr	646 (534-757)	1415 (1243-1587)	119%	122 (83-161)	285 (211-359)	133%
	Total	2240 (1884-2597)	5695 (5291-6099)	154%	360 (282-438)	1275 (1130-1420)	254%

* 95% Confidence Intervals in Parantheses

Table 3. Revision Shoulder Arthroplasty Cost Per Case and National Cumulative Cost, 2008-2018

Year	All Cause Revision Shoulder Arthroplasty		Septic Revision Shoulder Arthroplasty	
	Cost Per Case	Cumulative Cost	Cost Per Case	Cumulative Cost
2008	19,426 (18,251-20,600)	74 (62-87)	18,509 (16,103-20,915)	14 (11-16)
2009	19,441 (18,112-20,771)	96 (725-120)	20,239 (17,422-23,056)	16 (10-21)
2010	20,551 (18,635-22,466)	118 (845-152)	20,637 (18,456-22,817)	25 (17-34)
2011	19,453 (18,292-20,614)	111 (90-132)	20,420 (18,598-22,242)	22 (17-27)
2012	19,406 (18,554-20,258)	119 (107-131)	20,340 (18,607-22,074)	27 (23-30)
2013	19,727 (18,974-20,479)	131 (121-142)	20,936 (19,630-22,242)	30 (27-33)
2014	20,022 (19,228-20,816)	143 (131-155)	21,473 (19,967-22,980)	30 (27-34)
2015	19,880 (19,020-20,740)	166 (152-180)	22,433 (19,745-25,122)	40 (35-46)
2016	20,248 (19,429-21,067)	188 (174-203)	23,671 (21,671-25,671)	61 (54-67)
2017	20,052 (19,342-20,762)	205 (190-220)	23,298 (21,860-24,736)	64 (58-70)
2018	20,428 (19,675-21,181)	226 (210-241)	23,775 (22,374-25,177)	72 (66-79)
Percent Change	5%	203%	29%	406%

* 95% Confidence Intervals in Parantheses; Cumulative Cost Presented in Millions of Dollars (e.g., 14 million dollars)

Table 4. Projected Procedural Volume Estimates of Revision Shoulder Arthroplasty in 2030

		All Cause Septic Revision Shoulder Arthroplasty		Septic Revision Shoulder Arthroplasty	
		Poisson	Linear	Poisson	Linear
	Overall	32156 (31003-33353)	18381 (16202-20560)	15065 (13962-16254)	5466 (4280-6653)
	% Change [1]	189%	65%	391%	78%
Sex	Male	17584 (16677-18541)	9230 (8107-10353)	9325 (8421-10327)	3140 (2393-3887)
	Female	14868 (14137-15638)	9151 (7897-10405)	5848 (5218-6553)	2326 (1836-2816)
Age Groups	45-54 yr	1776 (1582-1993)	1403 (1119-1687)	564 (395-734)	1272 (1016-1593)
	55-64 yr	10053 (9363-10794)	5181 (4480-5881)	1641 (1224-2059)	5322 (4608-6146)
	65-74 yr	16094 (15146-17102)	7515 (6463-8566)	2171 (1670-2672)	8170 (7180-9296)
	≥75 yr	6179 (5730-6662)	3977 (3286-4668)	958 (708-1208)	1783 (1515-2099)

[1] Percent [%] Change compared to 2018

Table 5. Demographics and comorbidities of opioid use groups

Demographic	Opioid Naïve	<0-1 OME		1-5 OME		5-10 OMEs		10-25 OMEs		>25 OMEs	
	n (%)	n (%)	P-value	n (%)	P-value	n (%)	P-value	n (%)	P-value	n (%)	P-value
Total	16740 (56.94)	1840 (6.26)		4560 (15.51)		1826 (6.21)		1947 (6.62)		2487 (8.46)	
Age Group											
>45	1636 (9.77)	199 (10.82)	0.143	494 (10.83)	0.016	182 (9.97)	0.093	228 (11.71)	<0.001	399 (16.04)	<0.001
55-64	5942 (35.50)	651 (35.38)		1684 (36.93)		696 (38.12)		744 (38.21)		1046 (42.06)	
65-74	5359 (32.01)	549 (29.84)		1385 (30.37)		569 (31.16)		577 (29.64)		722 (29.03)	
75+	3803 (22.72)	441 (23.97)		997 (21.86)		379 (20.76)		398 (20.44)		320 (12.87)	
Sex											
Female	7781 (46.48)	893 (48.53)	0.094	2386 (52.32)	<.0001	989 (54.16)	<.0001	1133 (58.19)	<.0001	1375 (55.29)	<0.001
Male	8959 (53.52)	947 (51.47)		2174 (47.68)		837 (45.84)		814 (41.81)		1112 (44.71)	
Elixhauser Comorbidity Index											
0	3608 (21.55)	343 (18.64)	<0.001	829 (18.18)	<0.001	329 (18.02)	<.0001	334 (17.15)	<0.001	348 (13.99)	<0.001
1	5166 (30.86)	482 (26.20)		1251 (27.43)		456 (24.97)		424 (21.78)		559 (22.48)	
2	3964 (23.68)	458 (24.89)		1082 (23.73)		447 (24.48)		451 (23.16)		547 (21.99)	
3	2264 (13.52)	318 (17.28)		732 (16.05)		281 (15.39)		325 (16.69)		442 (17.77)	
4+	1738 (10.38)	239 (12.99)		666 (14.61)		313 (17.14)		413 (21.21)		591 (23.76)	
Tobacco Use											
No	15700 (93.79)	1711 (92.99)	0.181	4221 (92.57)	0.003	1697 (92.94)	0.155	1778 (91.32)	<0.001	2165 (87.05)	<0.001
Yes	1040 (6.21)	129 (7.01)		339 (7.43)		129 (7.06)		169 (8.68)		322 (12.95)	
Preoperative Injection											
None	13674 (81.68)	1446 (78.59)	<0.001	3552 (77.89)	<0.001	1428 (78.20)	<0.001	1467 (75.35)	<0.001	1836 (73.82)	<0.001
<30 days	412 (2.46)	71 (3.86)		141 (3.09)		69 (3.78)		94 (4.83)		117 (4.70)	
30-60 days	1181 (7.05)	134 (7.28)		399 (8.75)		164 (8.98)		179 (9.19)		277 (11.14)	
61-90 days	1473 (8.80)	189 (10.27)		468 (10.26)		165 (9.04)		207 (10.63)		257 (10.33)	
Arthroplasty Type											
Total	11835 (70.70)	1239 (67.34)	<0.001	3101 (68.00)	0.001	1239 (67.85)	0.002	1313 (67.44)	0.011	1638 (65.86)	<0.001
Reverse	3301 (19.72)	430 (23.37)		366 (20.04)		424 (21.78)		424 (21.78)		563 (22.64)	
Hemiarthroplasty	1604 (9.58)	171 (9.29)		460 (10.09)		210 (10.79)		210 (10.79)		286 (11.50)	

* P-value comparing opioid use group to opioid naïve patients
OME: Oral Morphine Equivalents

Table 6. Univariate Analysis of 90-Day Complications in OME Cohorts compared to Opioid Naïve Patients

Demographic	Opioid Naïve	<1 OME		1-5 OME		5-10 OMEs		10-25 OMEs		>25 OMEs	
	n (%)	n (%)	P-value	n (%)	P-value	n (%)	P-value	n (%)	P-value	n (%)	P-value
ED Presentation	1494 (8.92)	222 (12.07)	<0.001	502 (11.01)	<0.001	223 (12.21)	<0.001	251 (12.89)	<0.001	338 (13.59)	<0.001
Pain-related ED Presentation	135 (0.81)	12 (0.65)	0.925	39 (0.86)	0.746	30 (1.64)	<0.001	35 (1.80)	<0.001	52 (2.09)	<0.001
90-Day Hospital Readmission	554 (3.31)	63 (3.42)	0.795	173 (3.79)	0.110	90 (4.93)	<0.001	111 (5.70)	<0.001	173 (6.96)	<0.001
Non-home Discharge	812 (4.85)	103 (5.60)	0.160	265 (5.81)	0.009	144 (7.89)	<0.001	164 (8.42)	<0.001	154 (6.19)	0.004
Extended Length of Stay	2511 (15.00)	329 (17.88)	0.001	814 (17.85)	<0.001	397 (21.74)	<0.001	468 (24.04)	<0.001	604 (24.29)	<0.001
Revision Surgery	235 (1.40)	46 (2.50)	<0.001	92 (2.02)	0.003	34 (1.86)	0.120	50 (2.57)	<0.001	90 (3.62)	<0.001
Prosthetic Joint Infection	81 (0.48)	9 (0.49)	0.975	29 (0.64)	0.204	16 (0.88)	0.027	24 (1.23)	<0.001	39 (1.57)	<0.001
Wound Dehisence	94 (0.56)	12 (0.65)	0.624	29 (0.64)	0.557	14 (0.77)	0.274	22 (1.13)	0.003	29 (1.17)	0.000
Any Medical Complication [1]	1567 (9.36)	214 (11.63)	0.002	509 (11.16)	<0.001	219 (11.99)	<0.001	274 (14.07)	<0.001	349 (14.03)	<0.001
Thromboembolic Event	364 (2.17)	48 (2.61)	0.230	99 (2.17)	0.989	45 (2.46)	0.423	60 (3.08)	0.011	78 (3.14)	0.003

* P-value comparing opioid use group to opioid naïve patients

[1] Includes myocardial infarction, in-hospital mortality, acute kidney injury, sepsis, hemorrhage, *c. difficile* infection, pneumonia, stroke, a thromboembolic event (DVT or PE), or a wound infections (superficial or deep)

Table 7. Multivariable Analysis of 90-Day Complications in OME Cohorts compared to Opioid Naïve Patients

Demographic	<1 OME		1-5 OME		5-10 OMEs		10-25 OMEs		>25 OMEs	
	Odds Ratio	P-value	Odds Ratio	P-value	Odds Ratio	P-value	Odds Ratio	P-value	Odds Ratio	P-value
ED Presentation	1.33 (1.14-1.55)	<0.001	1.20 (1.07-1.33)	<0.001	1.33 (1.14-1.55)	<0.001	1.38 (1.19-1.60)	<0.001	1.48 (1.30-1.68)	<0.001
Pain-related ED Presentation	0.75 (0.41-1.36)	0.350	0.98 (0.68-1.40)	0.918	1.90 (1.27-2.84)	0.002	1.98 (1.35-2.89)	<0.001	2.22 (1.59-3.11)	<0.001
90-Day Hospital Readmission	0.97 (0.74-1.27)	0.839	1.06 (0.89-1.27)	0.461	1.38 (1.09-1.74)	0.006	1.58 (1.27-1.95)	<0.001	1.86 (1.55-2.23)	<0.001
Non-home Discharge	1.10 (0.88-1.37)	0.400	1.17 (1.01-1.36)	0.036	1.64 (1.35-2.00)	<0.001	1.75 (1.45-2.12)	<0.001	1.61 (1.33-1.95)	<0.001
Extended Length of Stay	1.21 (1.06-1.38)	0.004	1.20 (1.10-1.32)	<0.001	1.53 (1.35-1.73)	<0.001	1.74 (1.54-1.96)	<0.001	2.05 (1.84-2.28)	<0.001
Revision Surgery	1.69 (1.23-2.34)	0.001	1.39 (1.08-1.77)	0.008	1.29 (0.90-1.87)	0.162	1.72(1.25-2.35)	<0.001	2.27 (1.76-2.93)	<0.001
Prosthetic Joint Infection	0.95 (0.47-1.91)	0.899	1.24 (0.81-1.91)	0.310	1.69 (0.98-2.91)	0.056	2.33(1.46-3.71)	<0.001	2.76 (1.85-4.12)	<0.001
Wound Dehisence	1.10 (0.60-2.02)	0.739	1.06 (0.70-1.62)	0.765	1.28 (0.73-2.26)	0.384	1.86 (1.16-2.99)	<0.001	1.90 (1.23-2.93)	0.003
Any Medical Complication [1]	1.21 (1.04-1.41)	0.013	1.15 (1.04-1.28)	0.008	1.23 (1.05-1.43)	0.007	1.45 (1.26-1.67)	<0.001	1.52 (1.34-1.73)	<0.001
Thromboembolic Event	1.14 (0.84-1.56)	0.374	0.95 (0.76-1.20)	0.707	1.07 (0.78-1.47)	0.666	1.31 (0.99-1.74)	0.053	1.36 (1.05-1.75)	<0.001

* P-value comparing opioid use group to opioid naïve patients, 95% confidence intervals in parantheses

[1] Includes myocardial infarction, in-hospital mortality, acute kidney injury, sepsis, hemorrhage, c. difficile infection, pneumonia, stroke, a thromboembolic event (DVT or PE), or a wound infections (superficial or deep)

Adjusted for age, sex, surgery type, elixhauser comorbidity index, and tobacco use

Table 8. Survival Analysis of Prosthetic Joint Infection in Opioid-Use Groups compared to Opioid Naïve Patients

	Opioid Naïve	**<1 OME**		**1-5 OME**		**5-10 OMEs**		**10-25 OMEs**		**>25 OMEs**	
Events / Total Patients in Cohort	281/16740 (1.68%)	40/1840 (2.17%)		102/4560 (2.24%)		67/1826 (3.67%)		66/1947 (3.39%)		124/2487 (4.99%)	
Events per 100 patient years	0.69	0.91		0.89		1.42		1.39		2.10	
Unadjusted Hazard Ratio (HR) [1, 2]	[ref]	1.31 (0.94-1.82)	0.1141	1.30 (1.04-1.63)	0.0236	2.08 (1.59-2.71)	<0.001	2.00 (1.54-2.63)	<0.001	3.02 (2.44-3.73)	<0.001
Model 1		1.28 (0.92-1.78)	0.1513	1.27 (1.01-1.60)	0.0382	2.02 (1.54-2.64)	<0.001	1.93 (1.47-2.530)	<0.001	2.80 (2.25-3.49)	<0.001
Model 2		1.27 (0.91-1.77)	0.1573	1.28 (1.02-1.60)	0.0364	2.00 (1.53-2.62)	<0.001	1.93(1.47-2.53)	<0.001	2.83 (2.27-3.51)	<0.001
Model 3		1.28 (0.92-1.78)	0.1518	1.27 (1.01-1.59)	0.039	2.01 (1.54-2.63)	<0.001	1.93 (1.48-2.53)	<0.001	2.80 (2.26-3.49)	<0.001

[1] HR comparing opioid use group to opioid naïve patients

[2] Presented as HR (95% confidenced interval), p-value

Model 1: Cox model adjusted for elixhauser comorbidity index, age, sex, smoking status, and arthroplasty type ignoring proportional hazard (PH) violations

Model 2: Stratified cox model to adjust for PH violations of elixhauser index, smoking, and arthroplasty type

Model 3: Extended cox model to adjust for PH violations of elixhauser index, smoking, and arthroplasty type (elixhauser-time and age-time interaction terms)

Table 9. Survival Analysis of Revision Surgery in Opioid-Use Groups compared to Opioid Naïve Patients

	Opioid Naïve	**<1 OME**		**1-5 OME**		**5-10 OMEs**		**10-25 OMEs**		**>25 OMEs**	
Events / Total Patients in Cohort	462/16740 (2.76%)	55/1840 (2.99%)		192/4560 (4.21%)		79/1826 (4.33%)		91/1947 (4.67%)		168/2487(6.76%)	
Events per 100 patient years	1.15	1.25		1.70		1.68		1.94		2.89	
Unadjusted Hazard Ratio (HR) [1, 2]	[ref]	1.09 (0.83-1.44)	0.5432	1.49 (1.26-1.77)	<0.001	1.49 (1.17-1.89)	<0.001	1.69 (1.35-2.12)	<0.001	2.50 (2.09-2.98)	<0.001
Model 1		1.07 (0.81-1.41)	0.6508	1.46 (1.22-1.72)	<0.001	1.44 (1.13-1.83)	0.0027	1.61 (1.28-2.02)	<0.001	2.25 (1.88-2.70)	<0.001
Model 2		1.06 (0.80-1.41)	0.649	1.45 (1.23-1.73)	<0.001	1.44 (1.13-1.83)	0.0028	1.61 (1.29-2.03)	<0.001	2.24 (1.87-2.69)	<0.001
Model 3		1.07 (0.81-1.41)	0.6471	1.45 (1.23-1.72)	<0.001	1.44 (1.13-1.83)	0.0029	1.61 (1.28-2.02)	<0.001	2.25 (1.88-2.71)	<0.001

[1] HR comparing opioid use group to opioid naïve patients

[2] Presented as HR (95% confidenced interval), p-value

Model 1: Cox model adjusted for elixhauser comorbidity index, age, sex, smoking status, and arthroplasty type ignoring proportional hazard (PH) violations

Model 2: Stratified cox model to adjust for PH violations of elixhauser index and age

Model 3: Extended cox model to adjust for PH violations of elixhauser index and age (elixhauser-time and age-time interaction terms)

Table 10. Demographics and Comorbidities of Patients Receiving Preoperative Corticosteroid Injections

Demographic	No Injections	<30 days		31-60 days		60-90 days	
	n (%)	n (%)	P-value	n (%)	P-value	n (%)	P-value
Total	23403 (79.60)	904 (3.07)		2334 (7.94)		2759 (9.38)	
Age Group							
>45	2576 (11.01)	93 (10.29)	0.017	227 (9.73)	0.016	242 (8.77)	<0.001
55-64	8674 (37.06)	311 (34.40)		816 (34.96)		962 (34.87)	
65-74	7338 (31.35)	275 (30.42)		689 (29.52)		859 (31.13)	
75+	4815 (20.57)	225 (24.89)		602 (25.79)		696 (25.23)	
Sex							
Female	11273 (48.17)	486 (53.76)	0.001	1260 (53.98)	<0.001	1538 (55.74)	<0.001
Male	12130 (51.83)	418 (46.24)		1074 (46.02)		1221 (44.26)	
Elixhauser Comorbidity Index							
0	4723 (20.18)	160 (17.70)	<0.001	414 (17.74)	<0.001	494 (17.91)	<.0001
1	6755 (28.86)	227 (25.11)		639 (27.38)		717 (25.99)	
2	5546 (23.70)	211 (23.34)		555 (23.78)		637 (23.09)	
3	3365 (14.38)	158 (17.48)		383 (16.41)		456 (16.53)	
4+	3014 (12.88)	148 (16.37)		343 (14.70)		455 (16.49)	
Tobacco Use							
No	21730 (92.85)	826 (91.37)	0.091	2177 (93.27)	0.449	2539 (92.03)	0.114
Yes	1673 (7.15)	78 (8.63)		157 (6.73)		220 (7.97)	
Opioid Use Group							
Opioid Naïve	13674 (58.43)	412 (45.58)	<0.001	1181 (50.60)	<0.001	1473 (53.39)	<0.001
0-1 OMEs	1446 (6.18)	71 (7.85)		134 (5.74)		189 (6.85)	
1-5 OMEs	3552 (15.18)	141 (15.60)		399 (17.10)		468 (16.96)	
5-10 OMEs	1428 (6.10)	69 (7.63)		164 (7.03)		165 (5.98)	
10-25 OMEs	1467 (6.27)	94 (10.40)		179 (7.67)		207 (7.50)	
>25 OMEs	1836 (7.85)	117 (12.94)		277 (11.87)		257 (9.31)	
Arthroplasty Type							
Total	16367 (69.94)	598 (66.15)	0.009	1577 (67.57)	0.050	1823 (66.07)	<0.001
Reverse	4688 (20.03)	219 (24.23)		512 (21.94)		664 (24.07)	
Hemiarthroplasty	2348 (10.03)	87 (9.62)		245 (10.50)		272 (9.86)	

* P-value comparing injection group to those without an injection within 90 days of surgery
OME: Oral Morphine Equivalents

Table 11. Univariate and Multivariate Analysis of Prosthetic Joint Infection in those Receiving Preoperative Corticosteroid Injections

Demographic	No Injections	<30 days		31-60 days		60-90 days	
	n (%)	n (%)	P-value	n (%)	P-value	n (%)	P-value
Total in Group	23403 (79.60%)	904 (3.07%)		2334 (7.93%)		2759 (9.38%)	
Prosthetic Joint Infection	161 (0.69)	10 (1.11)	0.140	10 (0.43)	0.141	17 (0.62)	0.664
Odds Ratio (Adjusted)	[ref]	1.42 (0.74-2.70)	0.293	0.57 (0.30-1.09)	0.091	0.86 (0.52-1.43)	0.561

* P-value comparing injection group to those receiving no injections

Table 12. Survival Analysis of Prosthetic Joint Infection in those Receiving a Corticosteroid Injection

	No Injection	**<30 days**		**31-60 days**		**61-90 days**	
Events / Total Patients in Cohort	524/23403 (2.23%)	39/904 (4.31%)		53/2334 (2.27%)		64/2759 (2.32%)	
Events per 100 patient years	0.92	1.74		0.92		0.96	
Unadjusted Hazard Ratio (HR) [1, 2]	[ref]	1.89 (1.37-2.63)	<0.001	1.00 (0.76-1.33)	0.971	1.05 (0.81-1.35)	0.737
Model 1		1.69 (1.23-2.35)	0.002	0.94 (0.71-1.25)	0.685	1.02 (0.78-1.32)	0.875
Model 2		1.70 (1.23-2.36)	0.001	0.95 (0.71-1.25)	0.710	1.01 (0.78-1.32)	0.886
Model 3		1.67 (1.21-2.32)	0.002	0.95 (0.71-1.25)	0.700	1.03 (0.79-1.33)	0.852

[1] HR comparing opioid use group to opioid naïve patients

[2] Presented as HR (95% confidenced interval), p-value

Model 1: Cox model adjusted for elixhauser comorbidity index, age, sex, opioid use, smoking status, and arthroplasty type ignoring proportional hazard (PH)

Model 2: Stratified cox model to adjust for PH violations of elixhauser index, smoking, and arthroplasty type

Model 3: Extended cox model to adjust for PH violations of elixhauser index, smoking, and arthroplasty type (elixhauser-time and age-time interaction terms)

Table 13. Demographics and Comorbidities for those Receiving a Previous Shoulder Surgery

Demographic	No Previous Surgery	Previous Surgery	
	n (%)	n (%)	P-value
Total	9545 (85.14)	1666 (14.86)	
Age Group			
>45	668 (7.00)	246 (14.77)	<0.001
55-64	3199 (33.51)	742 (44.54)	
65-74	3223 (33.77)	479 (28.75	
75+	2455 (25.72)	199 (11.94)	
Sex			
Female	4752 (49.79)	925 (55.52)	<0.001
Male	4793 (50.21)	741 (44.48)	
Elixhauser Comorbidity Index			
0	1185 (12.41)	213 (12.79)	0.051
1	2459 (25.76)	390 (23.41)	
2	2468 (25.86)	405 (24.31)	
3	1679 (17.59)	319 (19.15)	
4+	1754 (18.38)	339 (20.35)	
Injection Group			
None	7580 (79.41)	1313 (78.81)	0.026
≤30 days	274 (2.87)	66 (3.96)	
31-60 days	760 (7.96)	146 (8.76)	
≥60 days	931 (9.75)	141 (8.46)	
Tobacco Use			
No	8770 (91.88)	1509 (90.58)	0.075
Yes	775 (8.12)	157 (9.42)	
Opioid Use Group			
Opioid Naïve	5905 (61.86)	697 (41.84)	<0.001
0-1 OMEs	674 (7.06)	68 (4.08)	
1-5 OMEs	1334 (13.98)	395 (23.71)	
5-10 OMEs	468 (4.90)	156 (9.36)	
10-25 OMEs	531 (5.56)	171 (10.26)	
>25 OMEs	633 (6.63)	179 (10.74)	
Arthroplasty Type			
Total	5685 (59.56)	814 (48.86)	<0.001
Reverse	3410 (35.73)	761 (45.68)	
Hemiarthroplasty	450 (4.71)	91 (5.46)	

* Chi-square p-value comparing those with and without a previous surgery
OME: Oral Morphine Equivalents

Table 14. Univariate and Multivariate Analysis of Prosthetic Joint Infection in those with a Previous Nonarthroplasty Shoulder Surgery

Demographic	No Previous Surgery	Previous Surgery	
	n (%)	n (%)	P-value
Total in Group	9545 (85.1%)	1666 (14.9%)	
Rate of Prosthetic Joint Infection	40 (0.42)	23 (1.38)	<0.002
Odds Ratio (Adjusted)	[ref]	2.75 (1.59-4.76)	<0.001

* P-value comparing injection group to those receiving no injections

Table 15. Survival Analysis of Prosthetic Joint Infection in those with a Previous Nonarthroplasty Shoulder Surgery

	No Previous Surgery	Previous Surgery	
Prosthetic Joint Infection (no. events/patients in cohort [%])	132/9545 (1.38)	51/1666 (3.06)	
Unadjusted Hazard Ratio (HR) [1, 2]		2.25 (1.62-3.11)	<0.001
Model 1	[ref]	1.91 (1.36-2.68)	0.002
Model 2		2.99 (1.84-4.85)	0.001

[1] HR comparing those with previous surgery to those without

[2] Presented as HR (95% confidenced interval), p-value

Model 1: Cox model adjusted for comorbidities, age, sex, injection status opioid use, smoking status, and arthroplasty type ignoring proportional hazard (PH) violations

Model 2: Extended cox model to adjust for PH violations

FIGURES

Figure 1. Flow Diagram of Patient Inclusion and Exclusion Criteria.

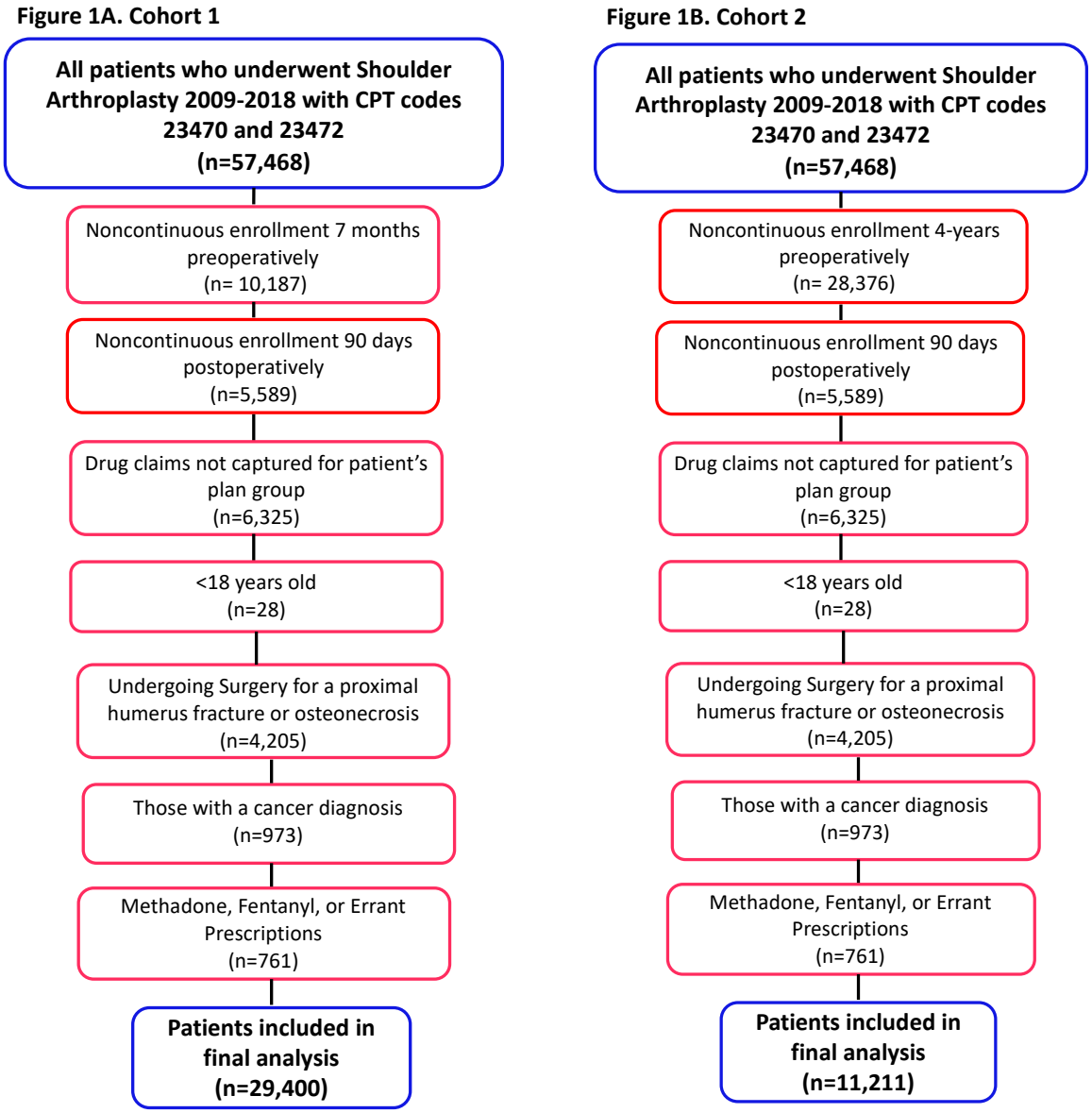

Figure depicting patient inclusion and exclusion criteria. All patients undergoing shoulder arthroplasty with CPT codes 23470 and 23472 from 2009-2018 were initially included. Subsequently, a number of exclusions were performed to arrive at cohort sizes used in final analysis. In Cohort 1 (**Figure 1A, left**), patients without continuous insurance enrollment in the 7-month preoperative period were excluded. In Cohort 2 (**Figure 1B, right**), patients without continuous insurance enrollment in the 4-year preoperative period were excluded. Other exclusion criteria were the same between cohort 1 and cohort 2.

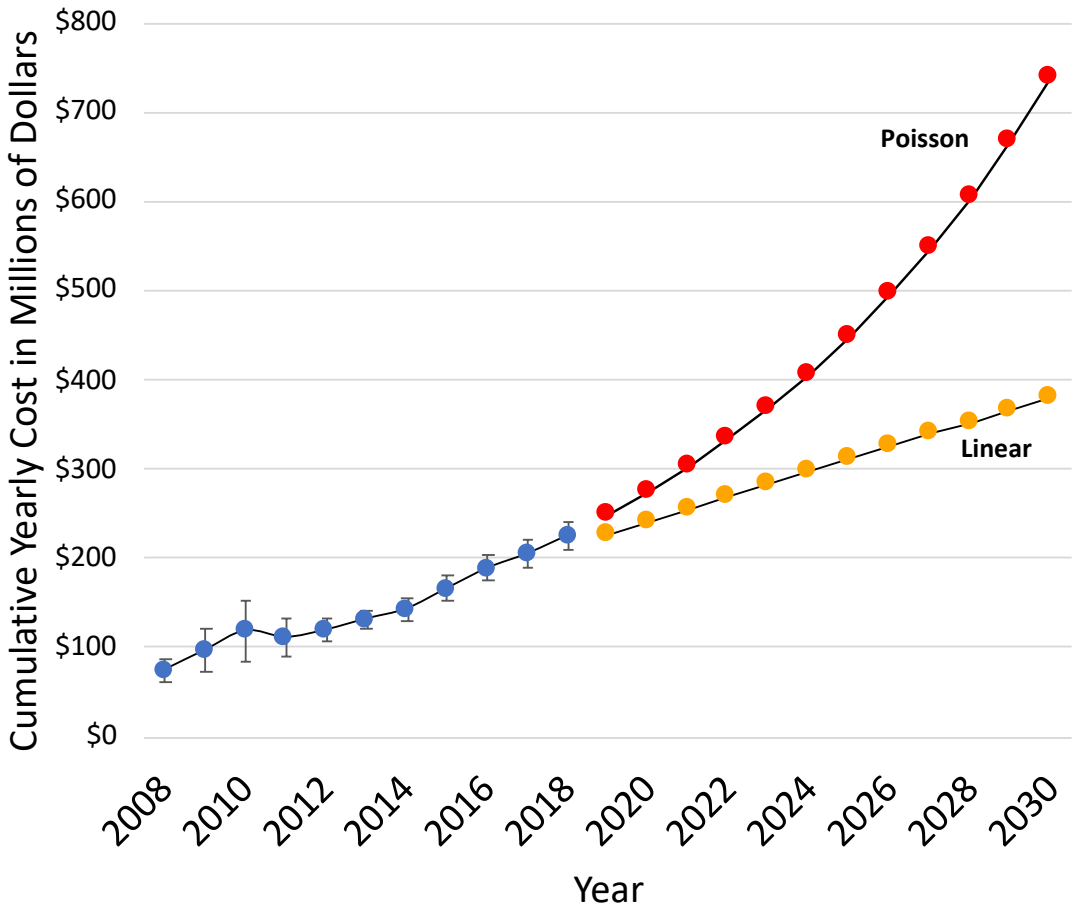

Figure 2. Yearly Cumulative Cost of All-Cause Revision Shoulder Arthroplasty in the United States, 2008-2030. Point estimates from 2008-2018 are displayed in blue. The linear projections and Poisson projections are displayed in yellow and red, respectively.

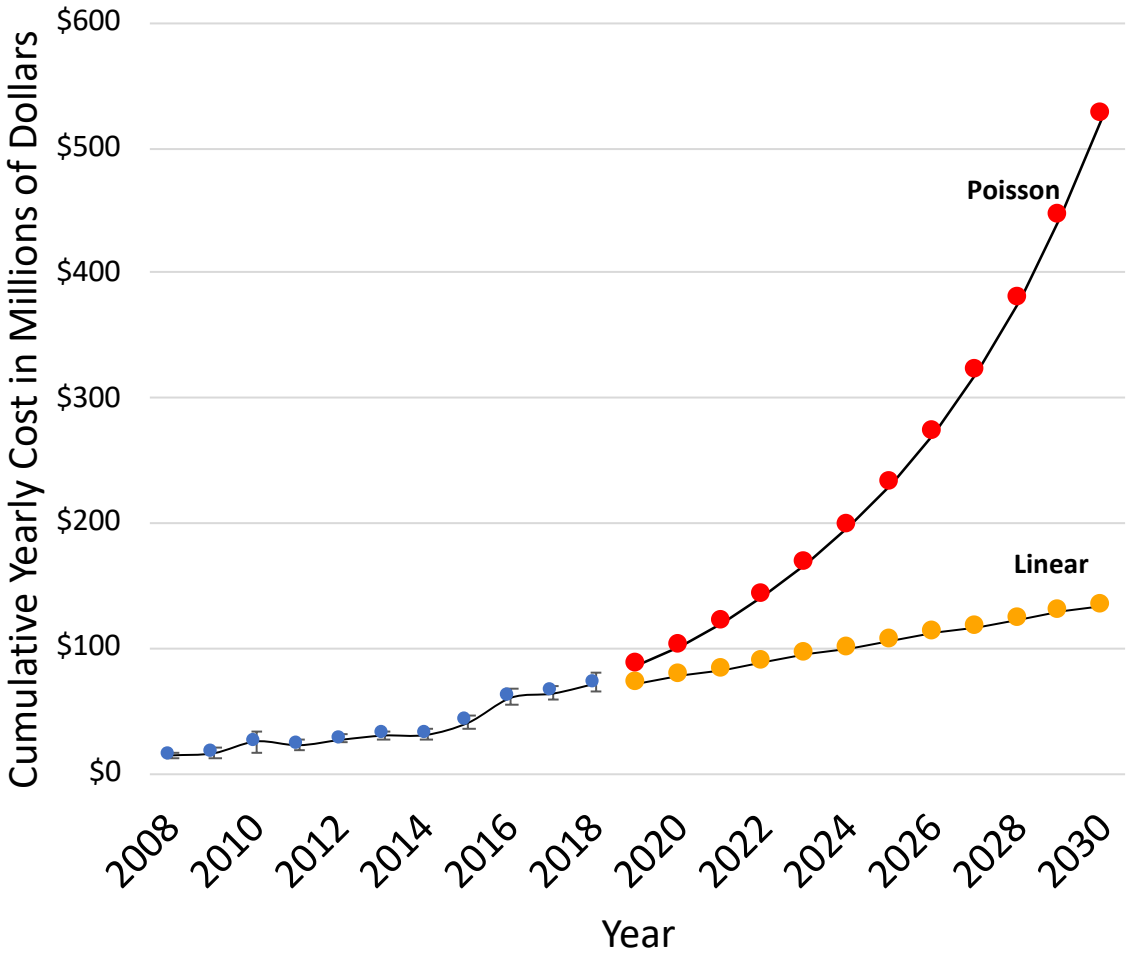

Figure 3. Yearly Cumulative Cost of Septic Revision Shoulder Arthroplasty in the United States, 2008-2030. Point estimates from 2008-2018 are displayed in blue. The linear projections and Poisson projections are displayed in yellow and red, respectively.

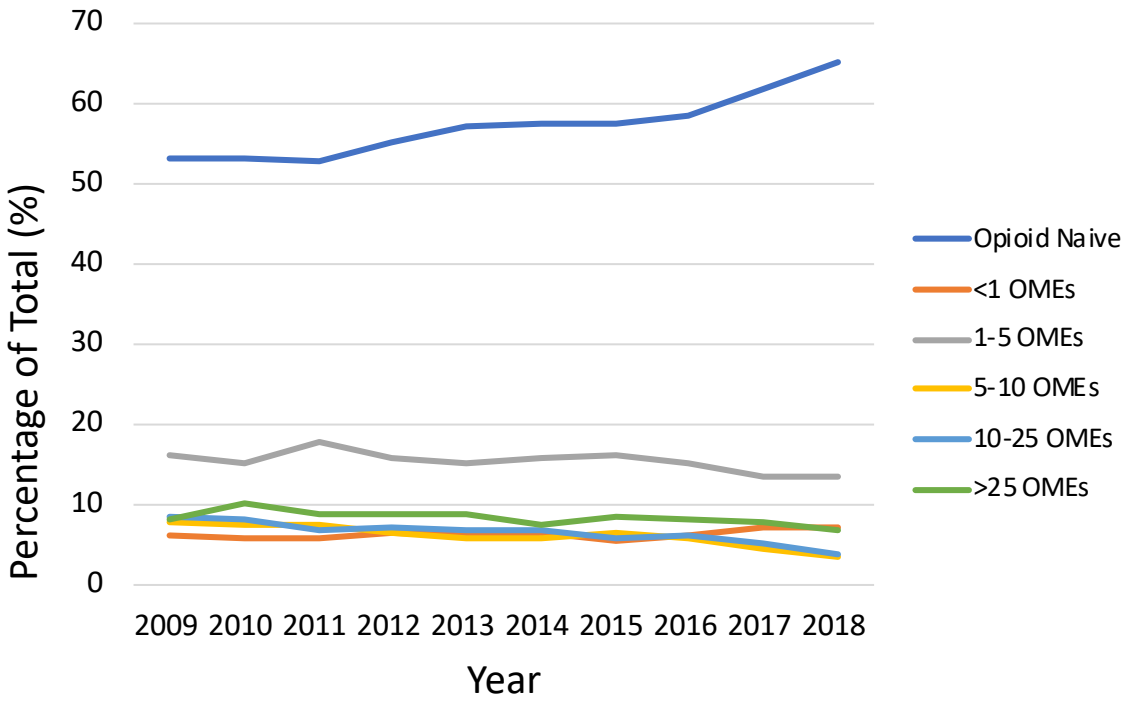

Figure 4. Trends of Pre-Operative Opioid Use in Patients Undergoing Primary Shoulder Arthroplasty, 2009-2018.